A number of groups reported that posterior pituitary peptides facilitate opiate tolerance and dependence (Cools et al 1977; de Wied & Gispen 1976; Krivoy et al 1974; van Ree & de Wied 1976; van Ree et al 1976). Recently, Walter et al (1978) reported an inhibition of morphine tolerance and physical dependence development in mice injected with a proposed competitive antagonist of PLG. In contrast, Schmidt et al (1978) found no effect of vasopressin or oxytocin on the level of tolerance attained after morphine pellet implantation for 3 days, or multiple i.p. injections for 5 days. One possible explanation of the difference in outcome is that the latter treatments produced maximal tolerance, and that the peptides increased the rate of acquisition but not the final degree of tolerance. This does not apply to the present results since they were obtained with the same methods as those used by van Ree & de Wied (1976). We have also found ambiguous effects of PLG and desglycinamide lysine vasopressin on the development of ethanol tolerance. In one study we found suggestions of impairment of tolerance by these peptides (Kalant et al 1978), but in a later unpublished replication we found no effect.

The subjects used by van Ree & de Wied (1976) were female rats while in the present study and in that of Schmidt et al (1978) they were male; therefore, the sex of subjects may prove to be a critical variable for understanding some peptide effects. However, in other experiments using male rats we found reproducible significant effects of neurohypophyseal peptides on ethanol consumption (Finkelberg et al 1978; Mucha & Kalant 1979). It seems probable that the effects of these peptides on acquisition of new behaviours are considerably more complex than has been so far recognized.

March 12, 1979

Note in Proof

Recently, Walter et al (1979) reported that PLG prevented rather than facilitated development of pellet-induced physical dependence on morphine in mice.

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The potassium ion selective electrode as a tetraphenylborate sensor for quaternary ammonium salts analysis

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Recently, some solid-state or liquid membrane selective electrodes, including the commercial calcium electrode (Orion, model 92–20), that have a Nernstian-like response to cationic detergents have been described (Baiulescu & Cosofret 1977). An especially prepared perchlorate selective membrane electrode was described (Vosta & Havel 1973) for potentiometric titrations of cetylpyridinium salts with perchlorate anion, but, due to the limited linear response region of the electrode, a relatively high concentration of quaternary ammonium compound (0·0235 M) was necessary for satisfactory analyses.

We have reported on potentiometric determinations of several quaternary ammonium compounds using a preconditioned silver electrode (Pinzauti & La Porta 1979). In a continuation of the applicability of potentiometry in cationic surfactants analysis, a commercial organophilic porous membrane electrode for potassium ion (Orion, model 93–19) was tested as indicating electrode using a standard 0·01 M sodium tetraphenylborate solution as the titrant.

2 ml of 0·2 M acetate buffer (pH 3·4) and 0·4 ml of 6 M NaCl solution were added to 20 ml of 0·0005–0·001 M stirred solution of cationic surfactant. The titrant was delivered in equal increments (0·025 ml) from a piston microburette (Metrohm, E457). Potentials of the potassium electrode were referred to a Metrohm EA404 saturated calomel electrode assembled into a Beckman remote junction filled with a 2 M NaCl solution. Potentiometric measurements were performed with a Metrohm E500 digital pH-meter capable of detecting change in potential of 0·2 mV. A typical titration curve is shown in Fig. 1; the end point was taken as the volume

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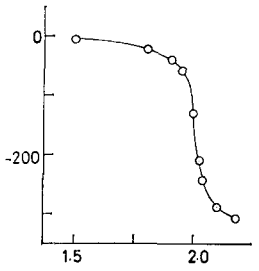

FIG. 1. Titration of 20 ml of 0·001 M cetylpyridinium chloride with 0·01 M sodium tetraphenylborate. Ordinate: E (mV). Abscissa: titrant (ml).

corresponding to the maximum $\Delta E/\Delta V$. The rise in the potential at the end point was about 70 mV per 0·025 ml of titrant (the reading in the end point region was usually taken after 2 min). Between titrations the potassium electrode was rinsed with water, soaked for 2 min in a stirred 0·01 M KCl solution, again rinsed with water and blotted dry. The good results of the determinations of four medicinally important quaternary ammonium compounds are presented in Table 1.

The possible interferent cations are reported in Orion's technical information on the potassium electrode, but no anion is quoted. With the previous Orion potassium ion selective electrode (model 92-19), the potentiometric titration of potassium with sodium tetraphenylborate was only moderately successful, apparently because the tetraphenylborate anion affected the electrode response (Lal & Christian 1970). When the present model of Orion potassium electrode was immersed in a buffered (pH 3·4) 0·0005 M KCl solution, the potential rapidly settled at −156 mV. If this calibrating solution was made up to contain a background concentration of tetraphenylborate anion (0·00005 M), a large negative shift up to −366 mV was observed (the solubility product of potassium tetraphenylborate is $2{\cdot}25 \times 10^{-8}$). The response of the potassium electrode to the teraphenylborate concentration in the ranges 10^{-2}–10^{-6} M was not Nernstian-like but we obtained a calibration curve (Fig. 2) with a maximum slope of about 126 mV in the range 1×10^{-4}–1×10^{-5} M; the time required for a stable response was about 3 min, but we obtained 97% of equilibrium response after 1 min. By taking advantage of the serious interference encountered with the tetraphenylborate ion, the potassium electrode can be converted to tetraphenylborate electrode and used as an indicator in the direct potentiometric titration of cationic surfactants which form very slightly soluble tetraphenylborate compounds.

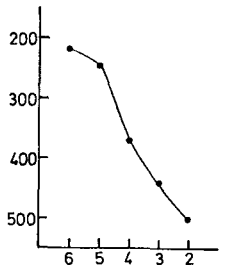

FIG. 2. Response of Orion potassium electrode to sodium tetraphenylborate in 0·1 M NaCl and 0·025 M acetate buffer at pH 3·4. Ordinate: E (−mV). Abscissa: −log [TPB⁻].

Table 1. Direct potentiometric determination of quaternary ammonium salts against 0·01 M sodium tetraphenylborate.

Compound	mg taken	Found % (s.d. on 6 samples)
Benzalkonium chloride	4·6–7·6	99·8 (0·3)
Benzethonium chloride	5·2–9·0	101·1 (1·2)
Benzyldodecylbis-(2-hydroxyethyl)-ammonium chloride	4·2–7·9	100·2 (0·1)
Cetylpyridinium chloride	3·8–7·2	100·6 (0·6)

The average electrode lifetime (a set of 4 potassium modules was employed) was 27 days ± 8 when used daily for the quaternary ammonium salts analyses. During their life the electrodes continued to exhibit Nernstian-like response in pure KCl solutions, but the calibration plot shifted to more positive potentials. The electrode failure (no response to tetraphenylborate excess) was sudden and low slope or no slope was then obtained towards potassium concentrations.

In preliminary experiments, titrations of quaternary ammonium salts with sodium laurylsulphate were unsuccessful, in fact, as for another commercial valinomycin based potassium electrode (Hammond & Lambert 1974), the potential of the Orion electrode is not affected by the anionic detergent.

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