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Electrochemical Determination of Electroinactive Medicines with Nafion-Coated Electrodes

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Amperometic determination of electroinactive medicines (acetylcholine, hexamethonium, neostigmine, quinidine and nicotine) based on partition effect has been successfully performed with a Nafion-coated electrode.

Du Pont's Nafion, a perfluoro sulfonated ion-exchange polymer, has been receiving a great deal of attention as a modifier for polymer coated electrodes mainly because of its outstanding chemical stability and excellent ionic conductivity. Among extensive studies, some attempts[1-3] have recently been made to use the Nafion-coated electrodes for determination of electroactive compounds. We report here the electrochemical determination of electroinactive cationic medicines based on the competitive partition between (ferrocenylmethyl)trimethylammonium ion (FA^+) and cationic medicines into Nafion layer. We have investigated several ammonium medicines and proved the effectiveness of the present method for determination of 10^{-6}-10^{-3} mol dm^{-3} level of these medicines.

A Nafion solution (Nafion 117, 1100 EW, 5% solution) was obtained from Aldrich Co. Cyclic voltammetry was carried out with a PAR model 273 at 25 °C. The working electrode was a glassy carbon disk (3 mm in diameter, GC-20, Tokai Carbon Co.) with a mirror-like surface.[3] Nafion coating was prepared by pipetting 2 µl of the 0.025% Nafion solution onto a clean surface and allowing the solvent to evaporate at room temperature.

The cyclic voltammetry of 7.2×10^{-6} mol dm^{-3} FA^+ on the Nafion-coated electrode showed near-ideal behavior of a thin film[4] with the apparent half-wave potential of 0.345 V vs. SCE. The concentration of FA^+ inside the Nafion membrane is susceptible to the presence of cationic medicines. The addition of the medicines resulted in decreases in the peak current for FA^+. These phenomena clearly demonstrate that some amount of FA^+ initially trapped inside the Nafion membrane is replaced by the medicines added to the electrolyte solution. Figure 1 shows the relationship between the relative peak current for FA^+ and the concentration of five medicines in the electrolyte solution. In this case, the peak current was recorded after 5 min of immersion of the Nafion-coated electrode into the solution. All medicines used here induced clear decreases of the relative peak current in the fairly low concentration ranges. The concentration of a medicine in a sample solution can be determined by using this relationships. The results are quite

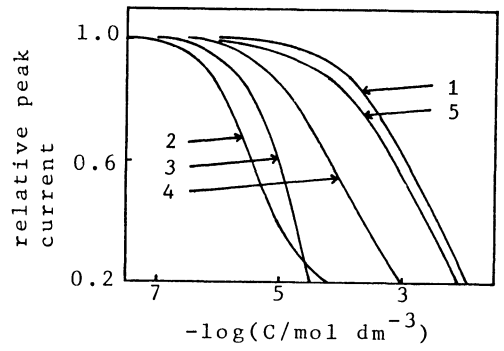

Fig. 1. Variation of relative peak current with concentration of medicines. Numbers correspond to the medicines in Table 1.

Table 1. Ion-selectivity coefficient (K) for ammonium medicines

Medicine	K
Acetylcholine (1)	5.6×10^{2}
Hexamethonium (2)[a)]	2.0×10^{5}
Qunidine (3)	1.0×10^{5}
Neostigmine (4)[b)]	2.8×10^{4}
Nicotine (5)	3.7×10^{3}
FA^{+}	7.3×10^{4} [2)]

a) Hexamethylene bis(trimethylammonium chloride). b) (Dimethylcarbamoyloxyphenyl)trimethylammonium bromide.

reproducible and the variations of the relative peak currents under different runs are within 5%. We have prepared relatively thin Nafion film (average thickness, 24 nm) to obtain quick responses. Since quinidine and nicotine are pH sensitive, a phosphate buffer (pH 7.0) was used as an electrolyte solution.

The present procedure is based on the competitive partitioning effect and thus the detection limit is largely dependent on the ion-selectivity coefficient;[5)] $K=x_M C_{Na}/(x_{Na} C_M)$ where x_M and x_{Na} are equivalent ionic fractions of SO_3^- sites in the Nafion layer occupied by the medicine and Na^+, respectively, and C's are the corresponding concentrations in an aqueous solution. The K values have been determined by voltammetry at a steady-state and are listed in Table 1. It is obvious that these medicines have strong affinity with Nafion. The value seems to be related with the hydrophobicity[6-8)] of the medicines. In a series of monocationic medicines relatively hydrophobic quinidine shows a large value whereas hydrophilic acetylcholine shows a small value.

Since all of these medicines employed here are electroinactive in a practical potential range, determination by direct electrochemical method is difficult. Futhermore, neither acetylcholine nor hexamethonium has a chromophore in the molecules and thus the determination by absorption spectroscopy is also difficult. It should be emphasized that the present procedure can be used for determination of these medicines and will be applicable to many cationic medicines.

References

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