Plasma-Polymerized Membrane Electrode for the Determination of Dextromethorphan and Dimenmorfan

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Ion-selective electrodes (ISEs) responsive to the antitussives dextromethorphan and dimenmorfan were constructed by the fixation of an ion-exchanger, ammonium tetraphenylborate, on a Millipore membrane by means of a plasma-polymerization technique. The electrodes showed a Nernstian response over the range of $10^{-8}$—$10^{-2}$ M dextromethorphan and dimenmorphan, and the working pH range was 5—7. The interference from common cations such as Na⁺, K⁺ and Ca²⁺ was negligible but some organic cations interfered weakly. The electrodes were applied successfully for the determination of the drugs in pharmaceutical preparations.

Keywords plasma-polymerized membrane; ion-selective electrode; dextromethorphan; dimenmorphan; potentiometric determination

Potentiometric methods are simple and rapid for pharmaceutical analysis when a suitable sensor is available, and many ion-selective electrodes have been successfully developed for the determination of various drugs such as ephedrine,1 sulfadiazine,2 quinine,3 cinemidine and ranitidine.4 Most of the electrodes reported are of the liquid membrane or polymer membrane type. The liquid membrane type is prepared by dissolving an ion-exchanger in an organic solvent,5 and the latter type is constructed by immobilizing wet membrane components containing the ion-exchanger within polymer membrane matrices.6 In both types of electrodes, however, there is a possibility of leakage of an ion-exchanger from the membrane phase, resulting in poor performance of the electrode as regards the detection limit7 and life time.8 Therefore, it would be worthwhile to attempt the fixation of ion-exchangers to the polymer matrix membrane.9

In a recent publication, some of the authors have reported on a new type of membrane electrode10 whose ion-exchangers were polymerized on a membrane filter by the plasma-polymerization technique. The polymerized membrane is strongly bound to the support and highly resistant to chemical and physical treatments.

In this paper, the construction of a plasma-polymerized membrane electrode responsive to dextromethorphan and dimenmorfan is described. The electrodes exhibited satisfactory sensitivity and selectivity for the determination of the drugs either in pure form or in pharmaceuticals.

Experimental

Materials Sodium tetraphenylborate (NaTPB) was purchased from Dojindo Laboratories. Dimethyl phthalate (DOP) was obtained from Nacalai Tesque and dextromethorphan hydrobromide was from Wako Pure Chemical. Difenmoran phosphate was a generous gift from Yamanouchi Pharmaceutical Co., Ltd. All chemicals used were of analytical reagent grade.

Membrane Preparation The apparatus and procedure for plasma-polymerization have been described previously.10 Briefly, NH₂TPB monomer was prepared by filtration of the precipitate formed from equimolar solutions of NH₂Cl and NaTPB. The monomer was vaporized at 60—75°C under an atmosphere of pure Ar of 10 Pa. The distance between the parallel-plate electrodes was 3.5 cm and the power of glow-discharge was 100 W at 13.56 MHz. The membrane for ISEs was prepared with the use of a Millipore filter (VSWP 02500, 0.025 μm nominal pore size, Bedford, Massachusetts) which served as the support for the plasma-polymerization. The plasma-polymerization was performed with a duration of discharge of 6 s, followed by soaking in DOP. After overnight soaking, the membrane was taken out and wiped with filter paper.

Potential Measurements The electromotive force (m.e.f.) across the plasma-polymerized membrane was measured by using the following cell: Ag, AgCl, KCl (saturated) || KCl (saturated) || reference solution || plasma-polymerized membrane || sample solution || KCl (saturated) || KCl (saturated), AgCl, Ag. An aqueous solution containing $10^{-2}$ M of drugs was used as the reference solution. All measurements of m.e.f. were made at 25 ± 1°C using an electrometer connected to a pen recorder. The sample and reference solutions were stirred throughout measurement.

Potentiometric Assay of Pharmaceutical Preparations An appropriate amount of dextromethorphan powder was dissolved in a 0.01 M H₂SO₄ solution by stirring for 1 h. The solution was diluted with water so as to obtain a final concentration in the range of $10^{-2}$—$10^{-4}$ M and the pH was adjusted to 6 by adding a small volume of NaOH solution. At least five tablets of dimenmorfan were powdered and a portion of the powder was dissolved in diluted sulfuric acid as described above. The concentration of the background electrolyte in the sample solutions was limited to about $10^{-2}$ M to minimize the effect of ionic strength. An aliquot (8 mL) of the resulting solutions was analyzed by the standard addition method and the calibration graph method.

Results and Discussion

Membrane potentials across the plasma-polymerized membrane are plotted against the logarithm of concentration of dextromethorphan and dimenmorfan in Fig. 1. The electrode exhibited a linear response with the slope of 59.1 mV/decade or 58.4 mV/decade at 25°C over the range...

![Fig. 1. Response Curve of the Plasma-Polymerized Membrane Electrode](image-url)

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of $10^{-2} - 10^{-5}$ M dextromethorphan or dimenofan, respectively. Dimenofan gave slightly greater sensitivity than dextromethorphan. The membrane potential reached a steady value within 5–10 s and was stable for several hours in the concentration range of $10^{-2} - 10^{-5}$ M. Below this level the response times were longer, but did not exceed 1 min in either case. The life time of these electrodes was at least 6 months, as reported previously for a plasma-polymerized membrane electrode.\(^{(10)}\) It was necessary, however, to store the membrane in DOP when it was not in use.

Effect of pH The effect of pH on the potential of the dextromethorphan electrode was examined by measuring the e.m.f. of the cell at $10^{-3}$ and $10^{-4}$ M dextromethorphan concentrations. The pH was varied by adding appropriate amounts of sulfonic acid and/or sodium hydroxide solution. As shown in Fig. 2, the electrode potentials were not affected by pH in the range of 5–7. The significant increase of the potential observed below pH 5 may be due to interference by H\(^+\), and the decrease of the potential above pH 7 is probably due to the increase of noncharged species arising from deprotonation, or the precipitation of the free base.

Selectivity of the Electrode The selectivity coefficients, \(K_i\), were evaluated according to the following equation,

\[
\Delta \Psi = \Delta \Psi_0 + \frac{(RT/F)\ln(C_0 + K_i C_i)}{C_0 + C_i}
\]

where \(C_0\) and \(C_i\) denote the concentrations of dextromethorphan and an interfering substance, respectively. \(\Delta \Psi\) is a potential change observed and \(\Delta \Psi_0\) is a constant. The potential change was measured in mixed solutions that contained either $10^{-3}$ or $10^{-4}$ M dextromethorphan solution and $10^{-2} - 10^{-5}$ M of the interfering substance. Selectivity coefficients obtained are presented in Table I. Negligible interference was found in the presence of common inorganic cations and amino acids. Weak interference was observed with some of the organic cations such as tetraethylammonium and atropine. Dimenofan interferes seriously, which is to be expected, as dextromethorphan and dimenofan have similar structures.

Assay of Dextromethorphan and Dimenofan in Pharmaceutical Preparations The drugs present in pharmaceutical preparations can be determined by the standard addition method after their dissolution in acidic solution.

### Table I. Selectivity Coefficients for Dextromethorphan Electrode

<table>
<thead>
<tr>
<th>Interfering species</th>
<th>Selectivity coefficient</th>
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<th>Selectivity coefficient</th>
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<tbody>
<tr>
<td>NaCl</td>
<td>$&lt;2.0 \times 10^{-4}$</td>
<td>Glycine</td>
<td>$&lt;4.0 \times 10^{-4}$</td>
</tr>
<tr>
<td>KCl</td>
<td>$3.8 \times 10^{-4}$</td>
<td>Histidine</td>
<td>$&lt;4.0 \times 10^{-4}$</td>
</tr>
<tr>
<td>NH(_4)Cl</td>
<td>$1.9 \times 10^{-3}$</td>
<td>Lysine</td>
<td>$&lt;4.0 \times 10^{-4}$</td>
</tr>
<tr>
<td>CaCl(_2)</td>
<td>$&lt;2.0 \times 10^{-4}$</td>
<td>Creatinine</td>
<td>$1.8 \times 10^{-3}$</td>
</tr>
<tr>
<td>Glucose</td>
<td>$2.0 \times 10^{-4}$</td>
<td>Acetylene</td>
<td>$&lt;4.0 \times 10^{-4}$</td>
</tr>
<tr>
<td>Urea</td>
<td>$2.0 \times 10^{-4}$</td>
<td>Atropine</td>
<td>$7.5 \times 10^{-3}$</td>
</tr>
<tr>
<td>(\text{C}_2\text{H}_5\text{NCl})</td>
<td>$2.3 \times 10^{-3}$</td>
<td>Dimenofan</td>
<td>1.7</td>
</tr>
</tbody>
</table>

### Table II. Determination of Dextromethorphan and Dimenofan in Pharmaceutical Preparations by the Standard Addition Method

<table>
<thead>
<tr>
<th>Compound</th>
<th>Content (mg/g or mg/tablet)</th>
<th>Nominal Found Recovery (%)</th>
<th>C.V. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medicom (Dextromethorphan powder)</td>
<td>100 102 103</td>
<td>10 10 101</td>
<td>3.3</td>
</tr>
<tr>
<td>Astomin (Dimenofan tablet)</td>
<td></td>
<td></td>
<td>3.6</td>
</tr>
</tbody>
</table>

The concentration (\(C_i\)) of the sample extracted from the commercial products was calculated from

\[
C_i = C_2 V_2 (\Delta \Psi (V_1 + V_2) - V_1)
\]

where \(V_1\) and \(V_2\) denote the volume and the concentration of added standard drug solution, respectively, \(\Delta \Psi\) is the potential change, \(S\) is the slope of the electrode response, and \(V_1\) is the volume of the initial sample solution.

The results of the assay for dextromethorphan in powder and dimenofan in tablets are presented in Table II. In both instances, the recovery was good and the coefficient of variation was less than 4%. The determination of 1–1000 \(\mu\)g/ml dextromethorphan in extracted solution was also done by the calibration graph method. The results obtained showed an average recovery of 101.6% of the nominal values, and the mean standard deviation was 3.2%. Thus, the new electrodes may provide a rapid and inexpensive method for the determination of dextromethorphan and dimenofan in pharmaceutical preparations.

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References