A novel ion selective PVC membrane electrode for determination of propranolol in pharmaceutical formulation

H.Y. Aboul-Enein* and Xian Xiang Sun

Introduction

Propranolol hydrochloride, 1-(isopropylamino)-3-(1-naphthoxy)-2-propanol hydrochloride, is a beta-adrenergic receptor blocking agent that is prescribed for its antihypertensive, antianxiety, anticonvulsant and antianginal effects. In some pharmacopoeia, propranolol hydrochloride is analyzed by titrimetrical method in non-aqueous media [1] (non-aqueous acidimetric method), spectrophotometric method [1-2], and high-performance liquid chromatographic method (HPLC) [2]. Numerous methods for the determination of propranolol hydrochloride in pharmaceutical formulation have been proposed in the literature, such as colorimetry and spectrophotometry [3-7], phosphorimetry [8], HPLC [9-11], kinetic determination [12], a.c. oscillographic titration [13] and conductometry [14]. In the non-aqueous titration method (acidimetric method), because of the small pH ranges which usually take place as the titration ends, it is difficult to apply this method for the determination of lower concentration range of the drug in the pharmaceutical preparations. Colored and turbid solutions interfere with the measurement of the absorbance in spectrophotometric method. Tedious sample preparation is often required in the chromatographic methods. Ion-selective electrodes (ISEs) or sensors have been considered as an attractive technique in the analysis of drugs due to the larger concentration range of analyte determined, reasonable selectivity, simple procedures which require no prior separation or sample preparation, and the accuracy of the analytical information [15,16]. For the determination of propranolol using ion-selective electrodes in pharmaceutical preparations, Zhang and co-workers [17] described the propranolol ion selective PVC membrane electrode in which the electroactive compounds or ion-pair complexes, propranolol-dinonyl naphthalenesulphonate (DNNS) or propranolol-tetra(2-chloro-phenyl) borate (CITPB), in the membrane, were obtained in situ by soaking DNNS/PVC or CITPB/PVC membranes in the propranolol solution. However, the long conditioning soaking time (24 h) of the electrode was required and a higher detection limit of \(2.5 \times 10^{-6}\) M of propranolol was reported. In this paper, the development of a novel propranolol ion-selective PVC membrane electrode is described. The electrode is successfully applied to analysis of propranolol hydrochloride in pharmaceutical formulation.

Experimental section

Reagents and materials

Propranolol hydrochloride was obtained in the pure raw material and in tablet dosage formulations from Changzhou Pharmaceutical Chemicals Works (Jiangsu, China). All reagents and solvents were of analytical reagent grade and deionized water was used throughout.
Standard solutions of propranolol hydrochloride were prepared by successive dilution of a 0.1 M stock solution which was obtained by dissolving 1.479 g propranolol hydrochloride in 50 mL of water.

**Preparation of the electroactive materials**

The propranolol-silicotungstate was used as the electroactive material in the membrane. It was prepared by dissolving 0.88 g of silicotungstic acid in 30 mL of water and mixing the solution of silicotungstic acid and 20 mL of 0.01 M propranolol hydrochloride solution. The resulting precipitate was filtered out on a porosity sintered-glass crucible (G4), washed with water and dried at 50 °C. The other electroactive component, propranolol-tetraphenylborate, was prepared in a similar way.

**Preparation of the electrode**

The mixture of the PVC cocktail was prepared by dissolving 4 mg of the propranolol-silicotungstate, 255 mg of high molecular weigh poly (vinyl chloride) (PVC), 141 mg of DNP in 2 mL of tetrahydrofuran, the membrane was prepared by pouring the mixture onto a glass petri dish (ca. 4 cm diameter) and allowed to stand overnight to dry at room temperature.

The PVC membrane electrode was fabricated using procedures that were previously described [18]. The Ag-AgCl electrode and 1.0 \( \times \) 10 \( ^{-3} \) M of propranolol solution were used as the reference electrode and the internal filling solution of the electrode, respectively. (The assembled electrode denoted as the electrode A). The other PVC membrane electrode (denoted as the electrode B), based on propranolol-tetraphenylborate used as the electroactive material and dibutyl phthalate (DBP) as the plasticizer (the PVC membrane compositions was 1.0:35.3:63.7 electroactive material: PVC: DBP respectively), was also assembled in a similar way.

The assembled electrodes were conditioned by soaking into 1.0 \( \times \) 10 \( ^{-3} \) M of propranolol hydrochloride solution for 3 h before the use of electrodes. When not in use, the electrodes were stored in air.

**Measurement of electromotive force (emf)**

The emf measurements were carried out at room temperature with a PXG-IB digital pH/mV meter (Jiangsu Electroanalytical Instrument Factory). A propranolol-selective PVC membrane electrode and a saturated calomel electrode (model 231) were used as indicating electrode and the reference electrode respectively. The test solutions were constantly stirred by a magnetic stirrer. The electrochemical cell was as follows:

S.C.E. / test solution / ISE.

**Analytical method for pharmaceutical formulations**

Not less than 10 propranolol hydrochloride tablets were weighed accurately crushed and mixed in a mortar. The sample solution was prepared as follows: a portion of the powder equivalent to 10 mg of propranolol hydrochloride was accurately weighed, and dissolved in 30 mL of water under stirring or sonicating condition. The resulting solution was transferred into a 50 ml volumetric flask, 5 mL of pH 5.5 acetate buffer solution was added, then completed to volume with water. The sample solution was transferred to a 100 mL breaker. The propranolol ion-selective membrane electrode and the reference electrode were immersed into the test solution. The emf reading was recorded. The amount of propranolol hydrochloride tablet was determined by using the calibration curve method.

**Results and discussion**

**Response characteristics of the electrodes**

The performances of the electrodes prepared with one of two ion-pair complexes, propranolol silicotungstate (electrode A) and propranolol tetraphenylborate (electrode B), as the electroactive materials in the membrane were experimentally compared. The results and the calibration graphs obtained with the two electrodes are shown in table I and figure 1.

From table I and figure 1, it is obvious that electrode A exhibits an excellent potential response properties such as the linearity range of 2.6 \( \times \) 10 \( ^{-2} \) ~ 3.0 \( \times \) 10 \( ^{-6} \) M and detection limit of 1.0 \( \times \) 10 \( ^{-7} \) M of propranolol hydrochloride and is performing much better, over one order of magnitude better than both electrode B and the electrodes based on fabrication with the use of either dinonylnaphthalene sulphonic acid or tetra (2-chlorophenyl) borate (potassium salt) as an electroactive site carrier in the membrane.

### Table I. Response characteristics of the electrodes.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Electrode A</th>
<th>Electrode B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Slope (mV per decade)</td>
<td>54.7</td>
<td>53.7</td>
</tr>
<tr>
<td>Linearity range (M)</td>
<td>2.6 ( \times ) 10 ( ^{-2} ) ~ 3.0 ( \times ) 10 ( ^{-6} )</td>
<td>1.0 ( \times ) 10 ( ^{-1} ) ~ 3.5 ( \times ) 10 ( ^{-5} )</td>
</tr>
<tr>
<td>Detection limit (M)</td>
<td>1.0 ( \times ) 10 ( ^{-7} )</td>
<td>1.0 ( \times ) 10 ( ^{-6} )</td>
</tr>
<tr>
<td>Equation</td>
<td>( Y = 54.72x + 293.1 )</td>
<td>( Y = 53.66x + 312.2 )</td>
</tr>
<tr>
<td>Correlation coefficient</td>
<td>0.9999</td>
<td>0.9964</td>
</tr>
</tbody>
</table>
Effect of pH

The effect of pH of the test solution (1.0 \times 10^{-3} M propranolol) on the response of the electrode was examined by measuring the variation in the emf with change in pH produced by the addition of very small volume of 0.01 ~0.1 M sodium hydroxide or hydrochloric acid solution into the test solution. Figure 2 showed that at a pH range of 2.5 ~8.0 and 4.0 ~7.5 for 10^{-3} M and 10^{-4} M propranolol solutions, respectively, no significant effect on the electrode potential were observed. At lower pH values (pH 4.0) the potential increased with decrease in the pH, presumably the electrode being sensitive to the diprotonated species. At higher pH values (pH 7.5) the potential decreased due to the precipitation of propranolol base [17]. Therefore, the electrode can be used at pH of 4.0 ~7.5 for propranolol determination.

Response time, stability and reproducibility

The response time of the electrode A was tested at 1.0 \times 10^{-1} ~1.0 \times 10^{-6} M of propranolol solutions and response time were about 5 s for 1.0 \times 10^{-3} M of propranolol solution and about 40 s for 1.0 \times 10^{-3} M of propranolol solution. The stability of the electrode response was monitored continuously at 1.0 \times 10^{-4} M of propranolol solution and evaluated for a period of 6 h; the potential drift was < 0.2 mV/h.

The repeatability of the potential reading for the electrode was examined by subsequent measurements in 1.0 \times 10^{-2} M of propranolol solution immediately after measuring the first set of solution at 1.0 \times 10^{-4} M of propranolol solution. The relative standard deviations for 6 replicate measurements obtained are 0.12 % for the solution of 1.0 \times 10^{-3} M and 0.23 % for the solution of 1.0 \times 10^{-3} M respectively. The electrodes were used at least for three months for serial calibrations and analytical applications.

Selectivity of the electrode

The selectivity of the electrode A was investigated by the separate solution method and calculated from the equation:

\[
\log K_{\text{PRO}^+, \text{J}^+} = \frac{E_j - E_1}{S} + 1 - \frac{1}{Z_j} \log [\text{PRO}^+] 
\]

where \( J^+ \) is the interfering ion, \( Z_j \) is the charge of the interfering ion; \( E_j \) and \( E_1 \) are the electrode potential 1.0 \times 10^{-3} M solution of the primary ion (PRO^+) and \( J^+ \), respectively, \( S \) is the slope of the calibration graph for the PRO^+ ion.

The potentiometric selectivity coefficients summarized in table II, show that all the inorganic compounds and most of the drugs, including metoprolol, do not affect the electrode behavior except for chlorphenamine and chlorpromazine. However, these two drugs are never associated with propranolol hydrochloride in pharmaceutical formulations. Accordingly, they do not influence the propranolol determination. Excipients in the propranolol tablets such as cornstarch, sugar, gelatin and magnesium stearate do not interfere.

Application to drug analysis

The reliability of the proposed propranolol-selective PVC membrane electrode for the quantification of propranolol...
was assessed by determining $2.0 \times 10^{-4}$ ~ $2.0 \times 10^{-3}$ M propranolol solution using the direct potential method. The recovery is shown in table III. In all cases the relative standard deviations were 2.2 %. The mean of recovery and the mean standard deviation were 102.0 % and 1.8 %, respectively.

The direct potential method was applied to the determination of propranolol hydrochloride in pharmaceutical tablets (ca. 10 mg propranolol hydrochloride/tablet, Changzhou pharmaceutical chemical works, batch number: 980506) and compared with the pharmacopoeia method (spectrophotometric method [2]). The mean value and the relative standard deviation obtained by using propranolol-selective membrane electrode method was 9.43 mg/tablet and 1.9 % ($n=6$) respectively. This is in good agreement with the value of 9.50 mg/tablet obtained by using spectrophotometric method.

### Conclusion

The electrode prepared with the ion pair complex of propranolol-silicotungstate as the electroactive material in the membrane has been successfully applied to the determination of propranolol hydrochloride in pharmaceutical formulations. The proposed method possesses many advantages such as fast response, lower detection of limit (< $10^{-6}$ M), good accuracy, adequate selectivity in the presence of related species and simple analytical procedures for the determination of propranolol hydrochloride in tablet formulation without the need for any sample preparation.

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### References

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