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Flow-injection pulse amperometric detection based on ion transfer across a water-plasticized polymeric membrane interface for the determination of verapamil

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Abstract

A flow-injection pulse amperometric method for determining verapamil, based on ion transfer across a plasticized poly(vinyl chloride) (PVC) membrane, was developed. A four-electrode potentiostat with ohmic drop compensation was used, while a flow-through cell incorporated the four-electrode and the membrane, which contained tetraphenylpyridinium tetraphenylborate. The influence of the applied potential and of the flow-injection variables on the determination of verapamil was studied. In the selected conditions, a linear relationship between current peak height and verapamil concentration over a range of 5×10^{-6} to 1×10^{-4} M verapamil was found. Good repeatability and between-day reproducibility were obtained. Some common ions and pharmaceutical excipients did not interfere. The method proposed has been applied satisfactorily to the determination of verapamil in pharmaceuticals and human urine.

Keywords: Interface between two immiscible electrolyte solutions; Pulse amperometry; Plasticized polymeric membrane; Verapamil determination; Flow-injection analysis

1. Introduction

Ion transfer across the interface between two immiscible electrolyte solutions (ITIES) has been widely studied. It is one of the main topics of the electrochemistry of liquid–liquid interfaces, for which several reviews [1–6], including those published periodically by Electrochimica Acta, have been reported. However, analytical applications are limited by the mechanical instability of the liquid–liquid interface. This drawback is especially important in flow systems. Stabilisation of the interface with a dialysis membrane [7,8] and, particularly, solidification of the organic phase with poly(vinyl chloride) (PVC) to become a polymer gel [9,10] which can be supported in an array of microinterfaces [11], or even a plasticized PVC membrane [12–17] similar to those used in ion-selective electrodes (ISEs) have widened the range of possible analytical applications. Flow-injection methodology has been used in several of these cases.

The typical 2:1 (m/m) plasticizer to PVC ratio used for ISEs provides membranes which are easy to handle, have a long lifetime and can be easily accommodated in ISEs bodies and flow-through cells. Their physical and chemical properties have been reviewed [18]. A significant advantage of amperometric transduction over classical potentiometric ISEs is that the ion selectivity of the former can be tuned by altering the magnitude of the applied potential. Another advantage is that the amperometric ISE, which provides a current response directly proportional to analyte concentration, is more suitable for detecting small changes in analyte concentration than the usual potentiometric ISE, which provides a potential response proportional to the logarithm of the analyte activity (concentration).

Verapamil is an antihypertensive agent belonging to the class of calcium channel blockers. Its generic name is verapamil hydrochloride, 5-[*N*-(3,4-dimethoxyphenylethyl)methylamino]-2-(3,4-dimethoxyphenyl)-2-isopropylvaleronitrile hydrochloride (Scheme 1).

Several methods for the determination of verapamil using different techniques, including spectrophotometry [19,20],

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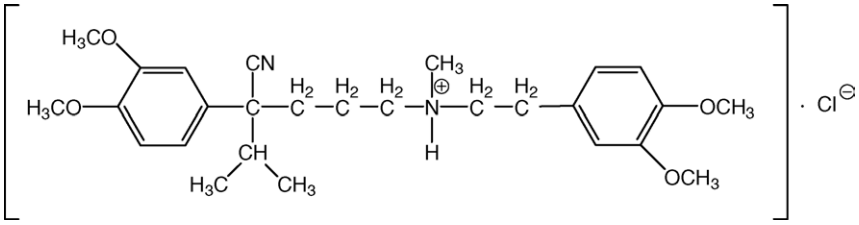

Scheme 1.

potentiometry with an ion-selective electrode [21], stripping voltammetry [22] and liquid chromatography [23,24] have been proposed.

In the present paper an amperometric method based on the transfer of verapamil ion across a water-plasticized polymeric membrane interface is proposed. An advantage of this approach over the voltammetric method involving the reduction of verapamil [22] is that removal of oxygen (which is time consuming) is not necessary.

2. Experimental

2.1. Apparatus

The four-electrode potentiostat and the four-electrode flow cell used were described in [16]. Ag/AgCl electrodes were used as reference electrodes and Pt electrodes were used as counter electrodes. A one-channel flow-injection assembly was used. The distance between the injection valve and the cell was 30 cm. A Merck Hitachi L-7110 isocratic pump, Omnifit injection valve, connecting tubing of 0.5 mm bore, PTFE tubing and various end fittings and connectors were used to construct the flow-injection system. A glass ring of 28 mm inner diameter and 30 mm height, glass plate, vial and punch were purchased from Fluka for the construction of the membranes.

2.2. Reagents and solutions

Poly(vinyl chloride) (PVC) high molecular mass, 2-nitrophenyl octyl ether (NPOE), sodium tetraphenylborate (NaTPB) and tetrahydrofuran (THF) were Selectophore products from Fluka. (±)Verapamil hydrochloride (VHCl) was purchased from Sigma. A 1×10^{-2} M solution of VHCl was prepared by dissolving in water. Working solutions were prepared by diluting with 5×10^{-2} M LiCl. Glucose, lactose, sucrose and starch were purchased from Probus. All the other reagents used were of analytical reagent grade. Nanopure water (18 MΩ) prepared with a Milli-Q (Millipore) system was used throughout.

1,2,4,6-Tetraphenylpyridinium perchlorate (TPPP) was prepared as described in [25].

1,2,4,6-Tetraphenylpyridinium tetraphenylborate (TPP^+ TPB^-) was precipitated by adding drop by drop a solution containing 0.1 g (0.2 mmol) TPPP dissolved in 3 ml acetone onto 20 ml of 0.01 M NaTPB (0.2 mmol). The precipitate was filtered off and recrystallised from ethanol.

1,2,4,6-Tetraphenylpyridinium acetate (TPPA) solution, 0.1 M, was prepared as described in [26].

Manidón tablets (Knoll, Spain): 80 mg verapamil hydrochloride, sucrose, lactose and other excipients. Manidón ampoules (Knoll, Spain): vial of 2 ml containing 5 mg verapamil hydrochloride, sodium chloride and distilled water.

2.3. Membrane preparation

The membranes were prepared by dissolving 200 mg NPOE, 100 mg PVC and 9.4 mg TPPTPB in 3 ml of tetrahydrofuran. This solution was poured into the glass ring resting on the glass plate and was left overnight to allow the solvent to evaporate slowly. A 7 mm diameter piece was cut out with the punch and incorporated into the flow-through cell. The electrochemical cell can be expressed as

$$\mathrm{Ag|AgCl|1 \times 10^{-2}\ M\ TPPA,\ 1 \times 10^{-2}\ M\ NaCl||5 \times 10^{-2}\ M\ TPP^{+}TPB^{-}||5 \times 10^{-2}\ M\ LiCl, \times M\ VHCl|AgCl|Ag}$$

The applied potential E is defined as the potential difference between the right and left hand terminals. E is controlled by means of the four-electrode potentiostat that applies the necessary potential between the right and left counter electrodes. A positive current corresponds to the transfer of positive charge from the right hand side to the left. This methodology, in which the potential difference at one membrane–solution interface is fixed by the common ion, has been used by several authors [27–29].

2.4. Flow-injection pulse amperometric procedure for the determination of verapamil

A 5×10^{-2} M LiCl carrier solution was pumped through the FI system at a flow rate of 1.75 ml min^{-1}. The potential applied to the detector cell was held at a base potential (E_b) of 195 mV, at which no current flows; voltage pulses of the same duration ($\tau = 0.25$ s) and amplitude ($\Delta E = E_f - E_b = 200$ mV or 100 mV) were applied at a constant interval ($\Delta t = 1$ s). The current was sampled and averaged during the last 25 ms of each pulse. For the determination of verapamil, 200 μl aliquots of working sample solutions (5×10^{-6}–1×10^{-4} M VHCl) were injected into the carrier solution. Calibration graphs were prepared by plotting the peak height versus VHCl concentration.