Potentiometric Determination of Betahistine in Pharmaceutical Formulations by Drug Selective Sensors

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Betahistine is histamine like drug that acts as both a partial histamine H1 receptor agonist and as a histamine H3 receptor antagonist. This research introduces design and construction of a PVC membrane sensor and nano-composite carbon paste electrode for fast and simple determination of Betahistine in pharmaceutical formulation. The best electrode performance was obtained with a membrane composition of 30% PVC, 63% NPOE, and 7% ion-pair and paste composition of 53% graphite, 30% paraffin oil, 15% ion-pair and 2% MWCNT. This electrode illustrated fast, stable and Nernstian response over a relatively wide concentration range of 1×10⁻⁵ to 1×10⁻² mol L⁻¹ for PVC membrane sensor and 1.0×10⁻⁶ to 5.0×10⁻¹ mol L⁻¹ for nano-composite carbon paste electrode. Validation of the method shows suitability of the sensors for application in quality control analysis of drug in pharmaceutical formulation.

Keywords: Betahistine, Potentiometry, Ion selective electrode, Ion-Pair complex, PVC membrane, Carbon paste

1. INTRODUCTION

Analysis of drugs by potentiometric sensors offers a fast, simple, inexpensive determination method. Potentiometric membrane sensors and carbon paste electrodes was widely used for determination of many ionic species [1-10]. Although potentiometric drug sensors are not sensitive as complex instruments, they can be easily made and are portable devices in comparison with them especially in assay of pharmaceuticals in formulations.
Betahistine (Fig. 1), 2-[2-(methylamino)ethyl]pyridine, is an anti-vertigo drug which is commonly prescribed to patients with balance disorders or to alleviate vertigo symptoms associated with Ménière's disease. Betahistine is a strong antagonist for histamine H\textsubscript{3} receptors and has a weak affinity as an agonist for histamine H\textsubscript{1} receptors. Betahistine has two modes of action. Primarily, it has a direct stimulating (agonistic) effect on H\textsubscript{1} receptors which are located on the blood vessels in the inner ear. This causes to local vasodilation and increase permeability, which helps to reverse the underlying problem of endolymphatic hydrops. And second, which is more important, is powerful antagonistic effects of Betahistine at H\textsubscript{3} receptors. It can increase the levels of neurotransmitters histamine, acetylcholine, norepinephrine, and serotonin released from the nerve endings. The increased amounts of histamine released from histaminergic nerve endings stimulate the receptors. This stimulation explains the potent vasodilatory effects of Betahistine in the inner ear [11].

Some analytical methods have been reported for the determination of Betahistine which include very few publications have been described for determination of Betahistine such as spectrophotometric methods and high performance liquid chromatographic (HPLC) [12], amperometric detector in capillary electrophoresis [13], and voltammetric assay [14]. Literature survey reveals that there is only one report on potentiometric determination of Betahistine in biological samples [15].

In comparison with complicated and time consumed techniques, potentiometric sensors offer the advantages of rapid, portable and inexpensive method of analysis. Although they cannot be considered as very accurate and precise methods in too complex matrixes, they can analysis pharmaceutics online and continuously without destructing the samples. Hence, they can be a good choice in study the dissolution or release profile of an active ingredient from the formulations or be useful devices in quality control section of a pharmaceutical factory.

In this work, a PVC membrane and a carbon paste electrodes have been designed and utilized for determination of Betahistine in some pharmaceutical formulations. Potentiometric electrodes are one of the subdivisions of electrochemical sensors which are widely used in analysis of various ionic species [16-30]. The most active ingredient of the sensor in both kinds of electrode is an ion-pair complex which was made from the interaction between Betahistine dihydrochloride and sodium tetraphenyl borate. The sensors respond according to the ion-exchange mechanism.

![Figure 1. Chemical structure of Betahistine](image-url)
of their advantages such as improved renewability, stable response, and low Ohmic resistance and no need for internal solutions. In addition, the best property of CPEs is ability to modify their compositions and can be made in any size easily.

2. EXPERIMENTAL SECTION

2.1. Materials and Reagents

Chemicals (of analytical reagent grade) were high-molecular weight polyvinylchloride (PVC) (Fluka Co., USA), sodium tetraphenyl borate (NaTPB), dibutyl phthalate (DBP), nitrobenzene (NB), benzyl acetate (BA), nitrophenyloctylether (NPOE), and tetrahydrofuran (THF) (Merck Co., Germany). Graphite powder with a <50 μm particle size (Merck Co., Germany), and 2.2 g/cm³ density along with the paraffin oil (Merck Co., Germany) of the highest purity were used for the preparation of the carbon pastes. The multi-wall carbon nanotubes (MWCNTs) with 10-40 nm diameters, 1-25 μm length, core diameter: 5-10 nm, SBET: 40-600 m²/g, V_total: 0.9 cm³/g, bulk density 0.1 g/cm³, true density 2.1 g/cm³ and with 95% purity were purchased from a local company (Iran). Betahistine dihydrochloride and its pharmaceutical formulation were obtained from Applied Chemistry Research Group, ACECR-Tehran branch (Iran). All materials were of the highest available purity without further modification.

2.2. Preparation of the ion-pair complex

Sensing material used in the membrane of the sensors was an ion-pair compound made from the interaction of Betahistine dihydrochloride and sodium tetraphenylborate. Sodium tetraphenylborate (NaTPB) is the organic compound with the formula of NaB(C₆H₅)₄. It is a salt, wherein the anion consists of four phenyl rings bonded to boron. This white crystalline solid is water soluble and can be used to prepare other tetraphenylborate salts, which are often highly soluble in organic solvents. The compound is used in inorganic and organometallic chemistry as a precipitating agent.

Ion-pair compound was prepared by mixing about 20 mL of 0.01 mol L⁻¹ solution of Betahistine dihydrochloride with 20 mL tetraphenyl borate solution (0.02 mol L⁻¹). Previous studies shows that TPB and Betahistine can form a 1:2 complex [15]. The resulting precipitate was then filtered, washed with distilled water and dried in room temperature for further usage [4,5,7,8].

2.3. Preparation of the sensors

PVC membrane sensor was prepared as follow: different amounts of ion-pair along with appropriate amounts of PVC, and plasticizer were dissolved in tetrahydrofuran (THF), and the solution was mixed well into a glass dish of 2 cm diameter. Then, THF was evaporated slowly until an oily concentrated mixture was obtained. A plastic tube (about 3 mm o.d.) was dipped into the mixture for about 10 s so a transparent membrane of about 0.3 mm in thickness was formed. The tube was
then pulled out from the mixture and kept at room temperature for about 4 h. Afterwards, the tube was filled with an internal filling solution (1.0×10⁻³ mol L⁻¹ of Betahistine dihydrochloride solution). The electrode was conditioned for about 20 h by soaking in the same solution [7,8].

General procedure for the preparation of carbon paste electrode was as follows: various amounts of ion-pair along with appropriate amount of MWCNTs (in case of modified carbon paste), graphite powder, and paraffin oil were thoroughly mixed. After homogenization of the mixture, the resulting paste was transferred into a plastic tube with 6 mm o.d. and a height of 3 cm. The paste was carefully packed into the tube tip to avoid possible air gaps, which often enhance the electrode resistant. A copper wire was inserted into the opposite end of the CPE to establish electrical contact. External surface of the carbon paste was smoothed with soft paper. The electrode was finally conditioned for about 48 h by soaking it in a 1.0×10⁻³ mol L⁻¹ of Betahistine dihydrochloride solution [17,19].

2.4. Betahistine standard solutions

Betahistine dihydrochloride is a white crystalline solid which is freely soluble in aqueous solutions. A solution of 0.1 mol L⁻¹ Betahistine dihydrochloride was prepared as stock solution. The working standard solutions (1×10⁻⁷ to 1×10⁻¹ mol L⁻¹) were then prepared by appropriately dilution of the stock solution with distilled water.

2.5. Apparatus

The glass cell where the Betahistine PVC membrane sensor was placed, consisted of two Ag/AgCl double junction reference electrodes (Azar-Eleelectrode Co., Iran) as internal and external reference electrodes. Both electrodes were connected to a Corning ion analyzer with a 250 pH/mV meter with ±0.1 mV precision.

The below cell assembly were used for potential measurements:

Ag-AgCl || internal solution, 1×10⁻³ mol L⁻¹ Betahistine dihydrochloride solution | PVC membrane | sample solution || Ag-AgCl, KCl (satd.)

In case of carbon paste electrode, a made carbon paste electrode was connected to an Ag/AgCl reference electrode by the same multimeter. The cell assembly was as follow:

Carbon paste surface | Betahistine dihydrochloride solution || Ag/AgCl, KCl (satd.)

These measurements were done using calibration method with several standard solutions.

2.6. Real sample analysis

Twenty tablets of Betahistine dihydrochloride finely powdered. Portions equivalent to the
weight of one, two and three tablets (each tablet contain 8 mg Betahistine) were weighed and transferred into a 100-mL volumetric flask. 50 mL of distilled deionized water was then added. The contents were shaken thoroughly to dissolve the compound, and then made up to volume and adjust the pH to 4.75 with acetate buffer (0.1 mol L⁻¹). Suitable aliquots of this solution were filtered through a Millipore filter (0.45 mm).

3. RESULTS AND DISCUSSION

In making potentiometric sensors the most important experimental parts is finding the best compositions of the membrane or the paste which cause the sensor responds according to the Nernst equation. Thus, the membrane ingredients or the paste ingredients should be optimized.

3.1. PVC Membrane Composition Selection

Amounts or type of the membrane ingredients which affect on the potential responses of the PVC membrane sensor was optimized. The main components of a liquid membrane are PVC matrix, plasticizer and the ion-pair as a sensing material. Each membrane component plays a special role in the membrane function and the sensor response.

Table 1. Selection of the membrane ingredients

<table>
<thead>
<tr>
<th>No.</th>
<th>PVC</th>
<th>Plasticizer</th>
<th>Ion-pair</th>
<th>Slopea (mV/decade)</th>
<th>LR (mol L⁻¹)a</th>
<th>DL (mol L⁻¹)a</th>
<th>Response time</th>
<th>R²</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>30</td>
<td>NPOE,67</td>
<td>3</td>
<td>18.5±0.6</td>
<td>1.0×10⁻⁴-1.0×10⁻³</td>
<td>1.0×10⁻⁴</td>
<td>1 min</td>
<td>0.977</td>
</tr>
<tr>
<td>2</td>
<td>30</td>
<td>NPOE,65</td>
<td>5</td>
<td>25.4±0.5</td>
<td>1.0×10⁻⁵-1.0×10⁻⁴</td>
<td>8.0×10⁻⁶</td>
<td>35 s</td>
<td>0.986</td>
</tr>
<tr>
<td>3</td>
<td>30</td>
<td>NPOE,63</td>
<td>7</td>
<td>29.7±0.3</td>
<td>1.0×10⁻⁵-1.0×10⁻⁴</td>
<td>3.2×10⁻⁵</td>
<td>20 s</td>
<td>0.998</td>
</tr>
<tr>
<td>4</td>
<td>30</td>
<td>NPOE,61</td>
<td>9</td>
<td>32.2±0.4</td>
<td>1.0×10⁻⁵-1.0×10⁻⁴</td>
<td>1.0×10⁻⁵</td>
<td>25 s</td>
<td>0.990</td>
</tr>
<tr>
<td>5</td>
<td>30</td>
<td>NB,63</td>
<td>7</td>
<td>10.7±0.7</td>
<td>1.0×10⁻⁵-1.0×10⁻⁴</td>
<td>1.0×10⁻⁵</td>
<td>1 min</td>
<td>0.911</td>
</tr>
<tr>
<td>6</td>
<td>30</td>
<td>DBP,63</td>
<td>7</td>
<td>24.1±0.5</td>
<td>1.0×10⁻⁵-1.0×10⁻⁴</td>
<td>1.0×10⁻⁵</td>
<td>42 s</td>
<td>0.992</td>
</tr>
<tr>
<td>7</td>
<td>30</td>
<td>BA,63</td>
<td>7</td>
<td>10.2±0.5</td>
<td>1.0×10⁻⁵-1.0×10⁻⁴</td>
<td>1.0×10⁻⁵</td>
<td>55 s</td>
<td>0.972</td>
</tr>
<tr>
<td>8</td>
<td>30</td>
<td>NPOE,70</td>
<td>0</td>
<td>2.9±0.8</td>
<td>1.0×10⁻⁴-1.0×10⁻⁷</td>
<td>1.0×10⁻⁴</td>
<td>2 min</td>
<td>0.855</td>
</tr>
</tbody>
</table>

*aThe results are based on five replicate measurements.

Previous studies shows that the membrane prepared with a plasticizer/PVC ratio about 2.2 can show the best performance [20-30]. Table 1 summarizes the most important prepared membranes. As it can be seen, the optimum amount of PVC was selected 30 mg and the best amount of plasticizer was 60 mg. Plasticizer should be a water-immiscible organic liquid which provide a homogeneous
dissolution and diffusional mobility of the ion-pair complex inside the membrane. The plasticizer should be an organic liquid with low vapor-pressure, compatible with PVC, no functional groups which can undergo protonation reactions. The nature of the used plasticizer can affect the analytical responses e.g. slope, linear domain and selectivity of the sensor. Four general plasticizers with different dielectric constants were used, including nitrobenzene (NB with DC of 35.7), nitrophenyloctyl ether (NPOE with DC of 24), dibutyl phthalate (DBP with DC of 6.4) and benzylacetate (BA with DC of about 5.7). The responses showed that the membrane had NPOE better responds. Since NPOE is rather a polar solvent and Betahistine ions are two valent ions [15] having a rather high charge density, NPOE among the used plasticizers provided an effective linear range and a lower detection limit due to the better extraction of Betahistine ions in the organic layer of the membrane.

As it can be seen from Table 1, absence of the ion-pair complex in the membrane causes a very poor response (membrane no. 8), which confirm the significance of the ion-pair complex. The best Nernstian slope was obtained 29.7±0.3 mV per decade with the membrane no. 3. This membrane composition was selected for the next experiments.

3.2. Carbon Paste Composition Selection

CPEs with a variety of compositions were prepared. The results for these CPEs are given in Table 2. The electrode composed of 30% paraffin oil, 15% ion-pair, and 55% graphite powder (no. 2) was found to be optimal for Betahistine carbon paste electrode. 15% ion-pair, 30% paraffin oil, 2% MWCNTs and 53% graphite powder (no. 5) was found to be optimal for Betahistine nano-composite carbon paste electrode.

Table 2. Selection of the carbon paste ingredients

<table>
<thead>
<tr>
<th>No.</th>
<th>Graphite (Wt.%</th>
<th>Paraffin (Wt.%</th>
<th>Ion-pair (Wt.%</th>
<th>MWCNT (Wt.%</th>
<th>Slope* (mV/decade)</th>
<th>LR (mol L⁻¹)*</th>
<th>DL (mol L⁻¹)*</th>
<th>Response time</th>
<th>R²</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>55</td>
<td>30</td>
<td>10</td>
<td></td>
<td>21.5±0.5</td>
<td>1.0×10⁻²-1.0×10⁻²</td>
<td>1.0×10⁻³</td>
<td>56 s</td>
<td>0.982</td>
</tr>
<tr>
<td>2</td>
<td>50</td>
<td>30</td>
<td>15</td>
<td></td>
<td>25.4±0.4</td>
<td>5.0×10⁻²-1.0×10⁻²</td>
<td>5.0×10⁻⁵</td>
<td>45 s</td>
<td>0.990</td>
</tr>
<tr>
<td>3</td>
<td>45</td>
<td>30</td>
<td>20</td>
<td></td>
<td>24.5±0.4</td>
<td>5.0×10⁻²-1.0×10⁻²</td>
<td>5.0×10⁻⁵</td>
<td>47 s</td>
<td>0.987</td>
</tr>
<tr>
<td>4</td>
<td>54</td>
<td>30</td>
<td>15</td>
<td>1</td>
<td>27.5±0.4</td>
<td>5.0×10⁻⁵-1.0×10⁻⁵</td>
<td>5.0×10⁻⁵</td>
<td>35 s</td>
<td>0.993</td>
</tr>
<tr>
<td>5</td>
<td>53</td>
<td>30</td>
<td>15</td>
<td>2</td>
<td>29.8±0.3</td>
<td>1.0×10⁻⁵-5.0×10⁻⁴</td>
<td>1.0×10⁻⁵</td>
<td>25 s</td>
<td>0.997</td>
</tr>
<tr>
<td>6</td>
<td>52</td>
<td>30</td>
<td>15</td>
<td>3</td>
<td>26.6±0.4</td>
<td>1.0×10⁻⁵-1.0×10⁻⁴</td>
<td>1.0×10⁻⁵</td>
<td>32 s</td>
<td>0.993</td>
</tr>
<tr>
<td>7</td>
<td>68</td>
<td>30</td>
<td>0</td>
<td>2</td>
<td>3.2±0.7</td>
<td>1.0×10⁻⁴-1.0×10⁻³</td>
<td>1.0×10⁻³</td>
<td>2.5 min</td>
<td>0.867</td>
</tr>
</tbody>
</table>

*The results are based on five replicate measurements.

High conductivity of MWCNT increases the dynamic working range and response time of the sensor. Addition of 2% MWCNT to the composition was found to increase the response to a Nernstian
slope of about 29.8 mV decade\(^{-1}\) (no. 5). This nano-composition electrode was selected for further examination. From Table 2, it was obvious that in the absence of ion-pair and presence of other components (no. 7), the response of the modified CPE was very low (slope of 3.2±0.7 mV/decade).

3.3. Calibration Graph and Statistical Data

The measuring range of a potentiometric sensor is the linear part of the calibration graph as shown in Fig. 2. For many electrodes the measuring range can extend from 1 molar to \(10^{-6}\) or even \(10^{-7}\) molar concentrations [16-30]. Calibration graph slope for PVC membrane sensor is 29.7 mV per decade of the Betahistine concentration and a standard deviation of ±0.3 mV after five replicate measurements. A linear response towards the Betahistine concentration was from \(1.0 \times 10^{-5}\) to \(1.0 \times 10^{-2}\) mol L\(^{-1}\). In this work, detection limit of the liquid membrane sensor was \(3.2 \times 10^{-6}\) mol L\(^{-1}\) which was calculated by extrapolating the two segments of the calibration curves. In case of CPE a linear range for the Betahistine concentration was from \(1.0 \times 10^{-6}\) to \(5.0 \times 10^{-1}\) mol L\(^{-1}\) with detection limit of \(1.0 \times 10^{-6}\) mol L\(^{-1}\).

![Calibration curve of PVC membrane sensor and CPE](image)

**Figure 2.** Calibration curve of PVC membrane sensor and CPE, the results are based on 5 replicate measurements

3.4. Dynamic Response Time

Dynamic response time is the required time for the sensor to achieve values within ±1 mV of the final equilibrium potential, after successive immersions in the sample solutions [25-28]. Its calculation involved the variation and the recording of the Betahistine concentration in a series of solutions from \(1.0 \times 10^{-5}\) to \(1.0 \times 10^{-2}\) mol L\(^{-1}\). Sensor was able to quickly reach its equilibrium response
in the whole concentration range. This time for the PVC membrane sensor was about 20 s and in case of CPE was about 25 s.

3.5. pH Effect on the Response

To examine the effect of pH on the electrode responses, the potential was measured at specific concentration of the Betahistine solution (1.0×10⁻⁴ mol L⁻¹) from the pH value of 1.0 up to 10.0 (concentrated NaOH or HCl solutions were employed for the pH adjustment) by PVC membrane electrode. The results showed that the potential remained constant despite the pH change in the range of 4.0 to 7.0, which indicates the applicability of this electrode in the specified pH range.

The fluctuations above the pH value of 7.0 might be justified by removing the positive charge on the drug molecule and decrease the solubility of the drug in aqueous solution. Fluctuations below the pH value of 4.0 were caused by removal of the membrane ingredients or analyte in the solution.

![Figure 4. Applicable pH of the electrodes in the test solution of 1.0×10⁻⁴ mol L⁻¹ (it was tested by PVC membrane)](image)

3.6. Life-time Study

The average lifetime for most of the reported potentiometric sensors is in the range of 4–10 weeks. Sensor lifetime was estimated by the calibration curve, periodical test of a standard solution and calculation of its response slope. For this estimation, three electrodes were employed extensively (1 hour per day) for 10 weeks. After 7 weeks utilization of the PVC membrane sensor, two changes were observed; a slight gradual decrease in the slope and an increase in the detection limit. It is well known that the loss of plasticizer, sensing element from the polymeric layer due to leaching into the sample solution after several times of usage, is a main reason for limited lifetimes of the sensors. In
case of carbon paste electrode has a longer life-time and can be used several times for a long time. By polishing the surface of the carbon paste a new surface exists and in fact a new electrode is generated.

3.7. Analytical Applications

Linearity, limit of detection, recovery test, selectivity, precision, accuracy, and ruggedness/robustness were the parameters used for the method validation.

The proposed sensor was evaluated by measuring the Betahistine concentration in some pharmaceutical formulations (Table 4) by the proposed sensors. The drug concentration was determined using calibration method. The results are in satisfactory agreement with the labeled amounts.

Selectivity, which describes an ion-selective electrode’s specificity toward the target ion in the presence of interfering ions, is the most important characteristic of these devices. The potentiometric selectivity coefficients of the Betahistine sensor were evaluated by the matched potential method (MPM) [29,30]. The resulting values of the selectivity coefficients are shown in Table 5. Note that all selectivity coefficients shows that the interferences negligible in the performance of the electrode assembly.

Table 4. Potentiometric determination of Betahistine hydrochloride in pharmaceutical formulations

<table>
<thead>
<tr>
<th>Sample</th>
<th>Stated content (mg/tab.)</th>
<th>Found by PVC membrane sensor* (mg/tab.)</th>
<th>Found by CP sensor* (mg/tab.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample 1</td>
<td>8</td>
<td>8.40±0.16</td>
<td>7.93±0.22</td>
</tr>
<tr>
<td>Sample 2</td>
<td>8</td>
<td>8.32±0.27</td>
<td>8.10±0.35</td>
</tr>
<tr>
<td>Sample 3</td>
<td>8</td>
<td>7.90±0.13</td>
<td>8.37±0.28</td>
</tr>
</tbody>
</table>

* The results are based on five replicate measurements.

Table 5. Selectivity coefficients of various interfering compounds for Betahistine sensors

<table>
<thead>
<tr>
<th>Interfering ion</th>
<th>Log (K_{MPM}) PVC membrane sensor</th>
<th>Log (K_{MPM}) Carbon paste sensor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na⁺</td>
<td>-3.0</td>
<td>-3.1</td>
</tr>
<tr>
<td>K⁺</td>
<td>-3.3</td>
<td>-3.3</td>
</tr>
<tr>
<td>NH₄⁺</td>
<td>-2.9</td>
<td>-3.0</td>
</tr>
<tr>
<td>Ca²⁺</td>
<td>-3.4</td>
<td>-3.3</td>
</tr>
<tr>
<td>Mg²⁺</td>
<td>-3.4</td>
<td>-3.4</td>
</tr>
<tr>
<td>Cl⁻</td>
<td>-3.2</td>
<td>-3.3</td>
</tr>
<tr>
<td>NO₃⁻</td>
<td>-3.8</td>
<td>-3.7</td>
</tr>
<tr>
<td>Lactose</td>
<td>-4.5</td>
<td>-4.4</td>
</tr>
<tr>
<td>Glucose</td>
<td>-4.3</td>
<td>-4.2</td>
</tr>
</tbody>
</table>
For repeatability monitoring, 3 standard samples were measured. The RSD% values by PVC membrane were 2.43, 3.12 and 2.78% and for carbon paste electrode were 2.31, 2.57 and 2.92%. For ruggedness of the methods a comparison was performed between the intra- and inter-day assay results for Betahistine obtained by two analysts. The RSD values for the intra- and inter-day assays in the cited formulations performed in the same laboratory by two analysts did not exceed 4.5% (PVC membrane) and 4.8% (CPE). On the other hand, the robustness was examined while the parameter values (pH of the solution and the laboratory temperature) changed slightly. Betahistine recovery percentages were good under most conditions, and not showing any significant change when the critical parameters were modified.

4. CONCLUSIONS

In the present work, two kinds of potentiometric sensor were constructed for determination of Betahistine hydrochloride in its pharmaceutical formulation. The sensors demonstrated advanced performance with a lower detection limit of 3.2×10⁻⁶ mol L⁻¹ and potential responses across the range of 1.0×10⁻⁵-1.0×10⁻² mol L⁻¹ for PVC membrane electrode and 1.0×10⁻⁶ to 5.0×10⁻¹ mol L⁻¹ with detection limit of 1.0×10⁻⁶ mol L⁻¹ for CPE. Both sensors respond based on ion-exchange mechanism. The best membrane sensor performance was achieved by a membrane composition of 30% PVC, 63% NPOE and 7% ion-pair complex. The best electrode performance in case of CPE was obtained with the paste composition of 53% graphite, 30% paraffin oil, and 15% ion-pair and 2%MWCNT. This electrode illustrated fast, stable and Nernstian response over a relatively wide concentration range. Validation of the method shows suitability of the sensors for application of quality control analysis of drug in pharmaceutical formulation.

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References

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