Potentiometric Determination of Mepivacaine Hydrochloride Local Anesthetic Drug in Pharmaceutical and Biological Fluids Using Ion Selective Electrode

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Abstract

The objective of this work is to determine mepivacaine hydrochloride (MPVHC) as local anesthetic drug. Modified carbon paste ion-selective electrode was used for the determination of MPVHC in different dosage forms and biological fluids. The study depends on potentiometric titration of MPVHC drug using modified carbon paste (MCPE) as end point indicator electrode. The effects of the paste composition, different conditioning parameters and foreign ions on the electrode performance were investigated and response time of the electrode has been studied. The results obtained showed that carbon paste electrode modified with sodium tetraphenyl borate-MPV ion pair gives the highest potential break at the end point, Nernstian slope, wide concentration range and lower detection limit than the reinckate-, phosphotungestic- and phosphomolybdic-MPV ion pairs. The fabricated electrode obtained Nernstian response of 57.74±0.67 mV decade⁻¹ in the concentration range of 3.1×10⁻⁷ - 1.0×10⁻¹ mol L⁻¹ for MCPE electrode. The electrode was found to be operating within the pH range of 3.0–8.0 and exhibited a fast response time (about 14 s), low detection limit of 3.1×10⁻⁷ mol L⁻¹ and long lifetime (98 days). The electrode showed high selectivity to the MPVHC drug in the presence of different organic, inorganic and amino acids. The electrode was successfully applied for the determination of MPVHC in pharmaceutical preparations and biological fluids (urine and plasma) with high percent recovery and low standard and relative standard deviation values. The results obtained applying this potentiometric electrode are comparable with British pharmacopeia. The method validation parameters were optimized and the method can be applied for routine analysis of MPVHC drug.

Keywords: Mepivacaine HCl; pharmaceutical analysis; Potentiometry; British pharmacopeia; Modified carbon Paste Electrode.

I. Introduction

Mepivacaine hydrochloride (MPVHC; Scheme 1), with chemical name 2-piperidinecarboxamide, N-(2,6-dimethylphenyl)-1-methyl, monohydrochloride [1] is a local anesthetic drug. The local anesthetic amide drug, mepivacaine (pKₐ = 7.6) was a member of the piperidoxylidide group. Its mechanism is to suppress nerve membrane ion flow to stabilize nerve cell membranes and then prevent impulse generation and conduction. This drug was extensively metabolized by the liver and excreted in the urine of animals and human [2].

Various analytical methods have been published for the determination of MPVHC drug in different dosage units and biological fluids using liquid chromatography HPLC [3-5], UV–spectrophotometric [6, 7], gas chromatography [8] and liquid chromatography–tandem mass spectrometric (LC–MS–MS) methods [9]. These methods are either time consuming involving multiple analysis or too expensive for most analytical laboratories [10, 11]. Potentiometric sensor can offer an inexpensive and convenient method for analysis of a lot of analytes in solution and provide acceptable sensitivity [12].

Ion-selective electrodes (ISEs) are one of the analytical potentiometric methods used for determination of inorganic and organic substances [13-17], which are capable of quantification and selectivity identifying various drugs within its excipients. ISEs have many advantages which give precise, accurate and fast determination of different...
ionic species. In addition, ISEs are non-destructive tools [18–20]. The carbon paste electrodes (CPEs) are suggested as useful end point indicator electrode in the potentiometric titration of drugs [21–26]. CPEs had the advantages of very low Ohmic resistance, very short response time in addition to the ease of fabrication and regeneration as well as long functional lifetime compared to PVC and coated wire electrodes. ISEs are one of the few techniques that can measure both positive and negative ions. In fact, a number of ion-selective electrodes for target cations and anions have been described [22, 27–32]. This study describes the preparation and potentiometric performance of mepivacaine-carbon paste (MPVHC-CPE) electrode based on mepivacaine-tetraphenyl borate (MPV-TPB) ion pair as electroactive material and tricresylphosphate (TCP) plasticizer. The parameters affecting the performance of the modified electrode were optimized. The linearity, limits of detection and quantification, percentage recovery, accuracy and precision were reported. The effect of interfering materials such as ascorbic, lidocaine, uric acid, picric acid, amino acids and some mono-, di- and trivalent metal ions were studied using separate solution and matched potential methods and the proposed electrode showed high selectivity towards the target drug. The electrode was found to give accurate and precise results for the determination of MPVHC in different pharmaceutical preparations and biological fluids (urine and plasma).

Experimental

**Pharmaceutical**

Mepivacaine HCl (MPVHC) standard material with Potency: 99.22 %, water content: 0.03% Batch No. 002-141002 and mepecaine-L 1.8 mL carpule local anaesthetic dental injections (Batch No. 5412198, Mfg. claimed to contain 36/0.11664 mg mepivacaine HCl /levonordefrin) were kindly provided by Alexandria Co. for pharmaceuticals, Alexandria, Egypt

Reagents

The work was done using analytical reagent grades and some of them were used as such without any further purification. Distilled water was used in all tests. Urea, starch, glucose, fructose, lactose, sucrose, maltose, glycine, picric acid and chloride salts of cobalt, manganese, calcium, copper, zinc, sodium, potassium, iron, nickel and cadmium were used as interfering ions. o-Nitrophenol octylether (o-NPOE) and sodium tetraphenylborate (NaTPB) were supplied from Aldrich. Ammonium reineckate (RN, Fluka), phosphotungestic acid (PTA, BDH) and phosphomolybdic acid (PMA, Fluka) were used. They were used for preparing ISE.

**Apparatus**

Potentiometric measurements were done using Jenway 3505 pH-meter. Silver-silver chloride double-junction reference electrode (Metrohm 6.0726.100) in conjugation with different ion selective electrodes was used. pH measurements were done using Thermo-Orion, model Orion 3 stars, USA. Prior to analysis, all glasswares used were washed carefully with distilled water and dried in the oven before use.

**Stock solutions**

Mepivacaine HCl solution

MPVHC stock solution was prepared by transferring an amount of MPVHC working standard accurately about 282.81 mg into 100-mL volumetric flask contained about 30-mL of water, stirring the solution until dissolved then completed to volume with distilled water to obtain stock concentration of 1.0×10⁻¹ mol L⁻¹ MPVHC.

Sodium tetraphenylborate solution (NaTPB)

NaTPB solution with concentration 1×10⁻² mol L⁻¹ was prepared by dissolving 1811 mg into 500 mL distilled water, pH adjusted to 9 using sodium hydroxide solution then completed to volume with distilled water. The obtained solution was standardized potentiometrically against standard (1×10⁻² mol L⁻¹) thallium (I) acetate solution [33].

Interfering ions solutions

A stock solutions with concentration 10⁻³ mol L⁻¹ for urea, starch, glucose, fructose, lactose, sucrose, maltose, glycine, picric acid and chloride salts of ammonium, cobalt, manganese, calcium, copper, zinc, sodium, potassium, iron, nickel, and cadmium were prepared by dissolving the suitable weights into 100 mL distilled water.

**Electrode preparation**

Carbon paste electrode preparation

Carbon paste electrode preparation

The synthesis of carbon paste electrode was done by mixing accurately weight 500 mg of highly pure graphite powder and plasticizer (0.2 mL of DOP, TCP, DBP, DOS or o-NPOE). The mixing is done in mortar and the resulted paste was used to fill the electrode body [34, 35]. A fresh surface was obtained by gently pushing the stainless-steel screw forward and polishing the new carbon-paste surface with filter paper to obtain a shiny new surface.

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Electrode performance characteristics

The calibration of the developed electrode to evaluate the characteristics of its performance was done by transferring 10 mL from serial solutions of MPVHC ranged from $1.0 \times 10^{-2}$ to $1.0 \times 10^{-1}$ mol L$^{-1}$ to 25 mL glass container, followed by dipping the electrode II with 7.5 mg MPV/TPB ion pair content. The amount of ion pair content was validated by determining potential break values at the end point as shown in Table (1). Three modified carbon paste electrodes containing 7.5 mg of MVP-RN (electrode VI), MVP-PTA (electrode VII) and MVP-PMA (electrode VIII) ion pairs were prepared and their performance was studied. Data listed in Table 1 showed that they give lower potential break values at the end point compared with electrode II.

Effect of ion pair content

The optimization of ion pair content to enhance the electrode performance depends mainly on the amount of ion pair content used to construct sensitive and selective electrode to size and charge of a particular ion. The sensitivity of the developed electrode for five portions as 5, 7.5, 10, 12.5 and 15 mg. The MPVHC concentration was tested by varying the amount of MVP/TPB ion pair content to determining potential breaks at the end point as shown in Table (1). Three modified carbon paste electrodes containing 7.5 mg of MVP-RN (electrode VI), MVP-PTA (electrode VII) and MVP-PMA (electrode VIII) ion pairs were prepared and their performance was studied. Data listed in Table 1 showed that they give lower potential break values at the end point compared with electrode II.

Electrode performance characteristics

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potential readings were recorded and the e.m.f. was plotted as a function of $p[\text{MPVHC}]$ (Figure 1). The studied modified carbon paste electrodes (electrodes II, VI, VII and VIII) using MVP-TPB, MVP-RN, MVP-PTA and MVP-PMA ion pairs content and TCP plasticizer showed linear response over the concentration range from $3.1 \times 10^{-7}$ to $1.0 \times 10^{-4}$, $1 \times 10^{-6}$ – $1 \times 10^{-4}$, $1 \times 10^{-6}$ – $1 \times 10^{-4}$ and $1 \times 10^{-3}$ – $1 \times 10^{-1}$ mol L$^{-1}$ with Nernstian slope of 57.72±0.67, 52.71±0.56, 47.93±1.16 and 43.82±1.24 mV decade$^{-1}$ and low detection limit of $3.1 \times 10^{-7}$, $1 \times 10^{-6}$, $1 \times 10^{-6}$ and $1 \times 10^{-3}$ mol L$^{-1}$ for electrodes II, VI, VII and VIII, respectively (Figure 1). Therefore, the fabricated electrode II is validated according to IUPAC regulations by evaluating the linearity range, lower limit of detection, lower limit of quantification, precision, accuracy and sensitivity as shown in Table (2).

**Effect of plasticizer**

Different types of plasticizers can be used in fabrication of the carbon paste electrode. The presence of plasticizer play main rule in linearity range, lifetime, stability and selectivity of the developed electrode to particular analyte, so the plasticizer must show high lipophobicity, no crystallization in the membrane and no oxidation. Plasticizer with high molecular weight affect the properties of the electrode where the plasticizers having lower hydrodynamic volumes increased the strengths, stiffnesses, and toughnesses of the paste. The amount of plasticizer affect the dielectric asymmetry of the paste so the proportion of plasticizer must be optimized to enhance the lifetime of the developed electrode [39, 40]. The chosen plasticizer for the developed electrode is tested by construct five electrodes with different plasticizer (DOP, DBP, DOS, o-NPOE and TCP). The obtained potentiometric titration curves using each electrode revealed that the highest potential breaks at the end point was observed with electrode having TCP as plasticizer which indicated the highest sensitivity to the change in the concentration of MPVHC using electrode with TCP plasticizer as shown in Figure (2).

**Table (1): Effect of MVP/TBP ion pair content on the performance characteristics**

<table>
<thead>
<tr>
<th>Electrode type</th>
<th>Ionophore content (mg)</th>
<th>End point (mL)</th>
<th>Recovery (%)</th>
<th>Potential break at the end point, (mV)</th>
<th>AE/AV (mV/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>electrode I (MVP-TPB)</td>
<td>5</td>
<td>2.97</td>
<td>99.0</td>
<td>74.0</td>
<td>375</td>
</tr>
<tr>
<td>electrode II (MVP-TPB)</td>
<td>7.5</td>
<td>2.99</td>
<td>99.7</td>
<td>211.0</td>
<td>1060</td>
</tr>
<tr>
<td>electrode III (MVP-TPB)</td>
<td>10</td>
<td>2.96</td>
<td>98.7</td>
<td>101.0</td>
<td>510</td>
</tr>
<tr>
<td>electrode IV (MVP-TPB)</td>
<td>12.5</td>
<td>2.97</td>
<td>99.0</td>
<td>127.2</td>
<td>640</td>
</tr>
<tr>
<td>electrode I (MVP-TPB)</td>
<td>15</td>
<td>2.95</td>
<td>98.3</td>
<td>136.0</td>
<td>685</td>
</tr>
<tr>
<td>electrode VI (MVP-RN)</td>
<td>7.5</td>
<td>2.87</td>
<td>96.6</td>
<td>63.7</td>
<td>289</td>
</tr>
<tr>
<td>electrode VII (MVP-PTA)</td>
<td>7.5</td>
<td>2.80</td>
<td>95.4</td>
<td>55.9</td>
<td>253</td>
</tr>
<tr>
<td>electrode VI (MVP-PMA)</td>
<td>7.5</td>
<td>2.72</td>
<td>93.8</td>
<td>47.8</td>
<td>201</td>
</tr>
</tbody>
</table>

**Effect of soaking time**

One of the factors impacting the developed electrode performance, which affect the selectivity and sensitivity of electrode to analyte, is the time of electrode surface dipped in the MPVHB/NaTPB ion pair suspended solution. This pretreatment procedure for the fabricated electrode depend on the time the electrode surface reaches equilibrium with a test solution interface where the ion exchange happens is studied by soaking the electrode for different time 0 (without), 5, 10, 15, 30 min, 1, 2, 4 and 8 h. The results concluded that the time needed to optimize the performance of modified carbon paste electrode II is 15 min at 25 °C. It is obvious from the results that the potential breaks at the end point decrease with increase soaking time as showed in Figure (3).

**Effect of pH on electrode performance**

The working pH range for constructed electrode is studied using MPVHC standard solution with concentration $10^{-3}$ and $10^{-1}$ mol L$^{-1}$ at different pH values varied from 1.0 to 10.0. The pH of solutions was adjusted using 0.1–1.0 mol L$^{-1}$ HCl and/or NaOH. The resulting potential readings cleared that the electrode response with TCP as plasticizer and MPV/TPB as ion pair content remains constant within the pH range from 3.0 to 8.0. The change in mV readings at pH less than 3.0 and more than 8.0 can be accounted to the presence of hydroxyl species in the solutions which affect the potential readings of electrode II as shown in Figure (4).

**Effect of temperature of the test solution**

The isothermal coefficient (dE/dt) of the studied electrode is evaluated using calibration plots made between the resulting electrode potential for test solutions and their concentrations were ranged from $10^{-1}$ to $10^{3}$ mol L$^{-1}$ of MPVHC with different
temperatures (10–60 °C). A straight line is plotted between standard electrode potential (E°) at different temperatures and (t-25) (Figure 5), where (t) was the temperature of the test solution in °C using Antropov’s equation [37] as:

$$E° = E°(25) + (dE°/dt)(t - 25)$$

where E°(25) is the standard electrode potential at 25 °C. The slope obtained from the straight line represent the isothermal coefficient (dE°/dt) of the studied electrode and the value of the isothermal coefficient (0.00038 mV/°C) indicated high thermal stability of the electrode (II).

Response time
The developed electrode was also validated by testing the response time which is the time that the electrode needed to reach steady potential readings. It is considered an important factor for the studied electrode to sense the change in the concentration of the measured analyte. The response time is studied by sudden change in the concentration of MPVHC from 1.0 × 10^{-6} to 1.0 × 10^{-3} mol L^{-1}. This study revealed that the constructed electrode has a response time of 14 sec for over the concentration range from 10^{-6} to 10^{-3} mol L^{-1} MPVHC concentration. These results reflect that the time needed for electrode (II) to make potentiometric titration with robust and a precise potential reading is fast as shown Figure (6).

Lifetime
Another characteristic future of ion selective electrode is studied which played an important role in the electrode validity for adequate quantification of MPVHC^{+} ion in a certain period of time. The lifetime of the constructed carbon paste electrode using TCP as plasticizer and MPV/TPB as ion pair is determined by potentiometric titration of 3 mL of 10^{-2} mol L^{-1} MPVHC with 10^{-2} mol L^{-1} NaTPB solution over a period of time reached to 122 days. The resulting potential break at the end point slightly decreased over this period and found that the electrode II is stable for 98 days as shown in Figure (7). After this time, the sensitivity of the electrode decreases due to decrease in the potential break at the end point. This could be due to leaching of paste components into tested solutions.

Selectivity
The selectivity of the developed electrode to only one species of analyte in the presence of interfering ions is one of the most vital features of the modified carbon paste electrode. Two methods are used to evaluate the selectivity coefficient of MPVHC electrode called separate solution method and the matched potential method [41]. First the separate solution method is used to study the selectivity coefficient of electrode in the presence of some common cations using 1 × 10^{-3} mol L^{-1} test solution of different cations at pH = 5, the value of selectivity coefficient (K_{selectivity}) was indicating how well the studied electrode can discriminate MPVHC^{+} against tested cations as obtained on the Table (3). Secondly matched potential method is used to evaluate the selectivity coefficient of MPVHC electrode in the presence of inorganic cations, anions, nitrogenous compounds such as starch, sugars and glycine, the numerical measurements of selectivity coefficient using an MPM exposed the high selectivity of constructing electrode and it is greater ability to distinguish the MPVHC^{+} from inorganic interfering ions as shown in Table (3).

Analytical Application
Application to pharmaceutical preparations
The fabricated electrode was fully validated and the results showed huge success for developed electrode in quantification of MPVHC in pure solutions and pharmaceutical dosage units. The ability of proposed electrode to quantify the MPVHC concentration in the bulk dosage form was tested by preparing three different concentrations of MPVHC in pharmaceutical formulations. The potential readings for the three levels of preparation samples provided great results as obtained on the Table (4), which ensure that the validated electrode has high selectivity, sensitivity and precise potential measurements. The values resulted from comparing the value of calculating t and F with tabulated values, demonstrating that there no significant dissimilarity between the developed and official method.

Application to biological fluids
The proposed electrode was used for determination of different concentrations of MPVHC in urine and human plasma samples. The developed electrode efficiency for accurate quantification of MPVHC in biological fluids in presence of interferences was studied by adding different known concentrations of MPVHC standard solutions to two different matrixes (urine and plasma samples). The results of potentiometric method are summarized in Table (5) which was indications for higher accuracy and selectivity of MVPHC-electrode to discriminate between MPVHC^{+} different concentrations and matrix components.
Table (2): Response characteristics of electrode II

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Electrode II</th>
</tr>
</thead>
<tbody>
<tr>
<td>Slope (mV decade$^{-1}$)</td>
<td>57.72 ± 0.672</td>
</tr>
<tr>
<td>Usable range (mol L$^{-1}$)</td>
<td>$3.1 \times 10^{-7}$</td>
</tr>
<tr>
<td>Detection limit (mol L$^{-1}$)</td>
<td>$3.1 \times 10^{-7}$</td>
</tr>
<tr>
<td>Quantification limit (mol L$^{-1}$)</td>
<td>$1.0 \times 10^{-7}$</td>
</tr>
<tr>
<td>Response time (s)</td>
<td>14</td>
</tr>
<tr>
<td>Working pH range</td>
<td>3 – 8</td>
</tr>
<tr>
<td>SD of slope (mV decade$^{-1}$)</td>
<td>0.38</td>
</tr>
<tr>
<td>Intersect (mV)</td>
<td>266.04 ± 2.93</td>
</tr>
<tr>
<td>Life time (days)</td>
<td>110</td>
</tr>
<tr>
<td>Accuracy (%)</td>
<td>99.96</td>
</tr>
<tr>
<td>Precision (%)</td>
<td>0.113</td>
</tr>
</tbody>
</table>

**Figure (1):** Calibration graph of MPVHC-MCPE electrode potentiometric sensor (electrode II).

**Figure (2):** Effect of plasticizer type on the performance of electrode II.

**Figure (3):** Effect of soaking time on the performance characteristics of electrode (II) in the potentiometric titration of 3 mL of $10^{-2}$ mol L$^{-1}$ MPVHC with $10^{-2}$ mol L$^{-1}$ NaTPB solution.

**Figure (4):** Effect of pH of the test solution on the performance characteristics of electrode (II).

Figure (5): Effect of temperature on the performance of electrode (II).

Figure (6): Dynamic response time of electrode (II).

Figure (7): Lifetime of electrode (II) based on the potentiometric titration of 3 mL of $10^{-2}$ mol L$^{-1}$ MPVHC with $10^{-2}$ mol L$^{-1}$ NaTPB solution

Table (3): Potentiometric selectivity coefficients of some interfering ions using electrode (II).

<table>
<thead>
<tr>
<th>Interfering ions</th>
<th>$-\log K_{\text{MPM}^{\text{MPVHC}}^{+}, \text{B}}$</th>
<th>Interfering ions</th>
<th>$-\log K_{\text{SSM}^{\text{MPVHC}}^{+}, \text{B}}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fructose</td>
<td>4.97</td>
<td>Na$^+$</td>
<td>3.28</td>
</tr>
<tr>
<td>Lactose</td>
<td>4.82</td>
<td>K$^+$</td>
<td>3.47</td>
</tr>
<tr>
<td>Sucrose</td>
<td>4.71</td>
<td>Co$^{2+}$</td>
<td>2.85</td>
</tr>
<tr>
<td>Maltose</td>
<td>4.86</td>
<td>Ni$^{2+}$</td>
<td>2.79</td>
</tr>
<tr>
<td>Glycine</td>
<td>4.29</td>
<td>Cd$^{2+}$</td>
<td>2.66</td>
</tr>
<tr>
<td>Urea</td>
<td>3.99</td>
<td>Cu$^{2+}$</td>
<td>2.48</td>
</tr>
<tr>
<td>Starch</td>
<td>4.02</td>
<td>Mn$^{2+}$</td>
<td>2.82</td>
</tr>
<tr>
<td>Glucose</td>
<td>4.17</td>
<td>Zn$^{2+}$</td>
<td>2.36</td>
</tr>
<tr>
<td>Picric acid</td>
<td>3.89</td>
<td>Ca$^{2+}$</td>
<td>2.29</td>
</tr>
<tr>
<td>Uric acid</td>
<td>3.19</td>
<td>Fe$^{3+}$</td>
<td>2.07</td>
</tr>
<tr>
<td>Lidocaine</td>
<td>1.08</td>
<td>Al$^{3+}$</td>
<td>2.14</td>
</tr>
<tr>
<td>Ascorbic acid</td>
<td>2.94</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

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Method validation
The method was validated for linearity, lower limit of detection, precision, accuracy, robustness and ruggedness in accordance with ICH guidelines [42, 43].

Linearity and lower limit of detection
Under optimal experimental conditions, the linearity of the proposed method was investigated by plotting the potential of the fabricated sensors/mV as a function of logarithm corresponding concentration of the tested MPVHC$^+$ ion. It has been shown that the fabricated sensors exhibit Nernstian response over the concentration range of $3.1 \times 10^{-7}$ to $1.0 \times 10^{-1}$ mol L$^{-1}$ with lower limits of detection of $3.1 \times 10^{-7}$ mol L$^{-1}$ for electrode (II) (Table 2). It is obvious that the use of MPV-TPB/ CPEs improve the sensitivity for detection of very small concentration of MPVHC$^+$ ion [16, 44, 45].

Precision and accuracy
In order to determine the precision of the proposed method, solutions containing concentrations of MVPHC were prepared and analyzed in four replicates and the analytical results are summarized in Table (6). The low values of the relative standard deviation (%RSD) also indicate the high precision and the good accuracy of the proposed method. RSD (%) and SD values were obtained within the same day to evaluate repeatability (intra-day precision) and over five days to evaluate intermediate precision (inter-day precision) [44, 46].

Table (5): Determination of MPVHC in spiked urine and human plasma using electrode (II)

<table>
<thead>
<tr>
<th>Sample</th>
<th>Statistical Parameters</th>
<th>Electrode</th>
<th>Direct method</th>
<th>Calibration method</th>
<th>Standard addition method</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>urine</td>
<td>Mean recovery (%)</td>
<td>99.75</td>
<td>99.56</td>
<td>99.00</td>
<td></td>
</tr>
<tr>
<td></td>
<td>N</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Variance</td>
<td>0.48</td>
<td>0.53</td>
<td>0.66</td>
<td></td>
</tr>
<tr>
<td></td>
<td>RSD (%)</td>
<td>0.36</td>
<td>0.31</td>
<td>0.40</td>
<td></td>
</tr>
<tr>
<td>Plasma</td>
<td>Mean recovery (%)</td>
<td>99.38</td>
<td>99.67</td>
<td>99.12</td>
<td></td>
</tr>
<tr>
<td></td>
<td>N</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Variance</td>
<td>0.46</td>
<td>0.49</td>
<td>0.51</td>
<td></td>
</tr>
<tr>
<td></td>
<td>RSD (%)</td>
<td>0.31</td>
<td>0.44</td>
<td>0.57</td>
<td></td>
</tr>
</tbody>
</table>

For urine sample: [MPVHC] taken = 0.75 mg L$^{-1}$. [MPVHC] found = 0.748, 0.747 and 0.743 mg L$^{-1}$ for direct, calibration and standard addition methods, respectively.

For plasma sample: [MPVHC] taken = 0.85 mg L$^{-1}$. [MPVHC] found = 0.845, 0.847 and 0.843 mg L$^{-1}$ for direct, calibration and standard addition methods, respectively.
Table 6: Evaluation of intra- and inter-days precision and accuracy of using electrode (II)

<table>
<thead>
<tr>
<th>Sample No.</th>
<th>MPVHC Taken, (mg/mL)</th>
<th>Intra day</th>
<th>Inter day</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MPVHC Found, (mg/mL)</td>
<td>Recovery* (%)</td>
<td>SD</td>
</tr>
<tr>
<td>Pure</td>
<td>0.25</td>
<td>0.246</td>
<td>98.4</td>
</tr>
<tr>
<td>1</td>
<td>0.25</td>
<td>0.245</td>
<td>98.0</td>
</tr>
<tr>
<td>3</td>
<td>0.5</td>
<td>0.471</td>
<td>94.2</td>
</tr>
</tbody>
</table>

By investigating the reproducibility of the results obtained, the ruggedness of the proposed method was carried out. It was done by the analysis of the same samples under different conditions such as analysts, different instruments and laboratories. For this purpose, the results obtained using another model of pH-meter (HANNA 211, Romania) was compared with those obtained using Jenway 3505 pH-meter. It was concluded that the results obtained were close and also revealed validity of the method [44, 46].

Comparison of Previous Works with the Current Study
A comparative study of the response characteristics of the proposed electrode (II) with some of the previously reported sensors for MPVHC is shown in Table 7. It is obvious for the data listed in this table that the proposed electrode (II) were superior over the previously reported sensors in terms of working concentration range, pH range, lifetime and Nernstian slope [47, 48].

Table 7: Comparing some of the MPV-TPB (electrode II) (characteristics with some of the previously reported MPVHC-ISEs).

<table>
<thead>
<tr>
<th>References</th>
<th>Slope (mV decade⁻¹)</th>
<th>Response time (s)</th>
<th>pH</th>
<th>Life time (days)</th>
<th>Linear range (mol L⁻¹)</th>
<th>DL (mol L⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proposed electrode</td>
<td>57.72</td>
<td>14</td>
<td>3 – 8</td>
<td>110</td>
<td>3.1×10⁻⁷ – 1.0×10⁻¹</td>
<td>3.1×10⁻²</td>
</tr>
<tr>
<td>47</td>
<td>54.08</td>
<td>&lt;30</td>
<td>3.5 - 7.0</td>
<td>-</td>
<td>5.0×10⁻³ – 1.0×10⁻²</td>
<td>5.0×10⁻⁵</td>
</tr>
<tr>
<td>48</td>
<td>56.08</td>
<td>10-20</td>
<td>3.5–6.5</td>
<td>-</td>
<td>5.0×10⁻⁵ – 1.0×10⁻²</td>
<td>5.0×10⁻⁵</td>
</tr>
</tbody>
</table>

Conclusion
The modified carbon paste electrode used in the quantification of mepivacaine HCl shows high accuracy, selectivity, sensitivity, short response time and long lifetime. The constructed electrode succeeds to determine MPVHC in pure solutions, pharmaceutical preparations and biological fluids without the fear that the presence of interference resulted from excipients in pharmaceutical preparations or matrix components in biological fluids affect the accurate quantification of MPVHC. The proposed potentiometric procedure proved its capability for adequate quantification of MPVHC with low cost and simple techniques to construct electrode compared to other analytical methods.

References

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