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A New Potentiometric Sensor for Determination of Pethidine Hydrochloride in Ampoules and Urine

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Abstract

A simple, precise, rapid and low-cost potentiometric method for pethidine determination in pharmaceuticals and urine is proposed. A chemically modified carbon paste electrode (CMCPE) for pethidine hydrochloride (PDCl) based on pethidine-phosphotungstate (PD-PT) as ion-pair complex was prepared and fully characterized in terms of composition, usable pH range, response time and temperature. The pethidine electrode showed Nernstain responses in the concentration range 2.1×10^{-6} - 1.0×10^{-2} M with a detection limit of 7.3×10^{-7} and usable within the pH range 3.5 - 6.6. This sensor exhibited a fast response time (about 5 - 8 s), good stability. The value (dE/dt) of the electrode was found to be 0.00071 V/°C, which indicates fairly high thermal stability. Selectivity coefficients determined by matched potential method (MPM) and separate solution method (SSM) showed high selectivity for PDCl with respect to a large number of inorganic cations, organic cations, sugars and some common drug excipients. The sensor could be used successfully in the estimation of PDCl in ampoules and in spiked urine samples.

Keywords: Potentiometry, Carbon Paste Electrode, Pethidine, Ion-Selective Electrode

1. Introduction

Pethidine (Meperidine hydrochloride, Dolantin) (Ethyl, 1-methyl-4-phenylpiperidine-4-carboxylate hydrochloride), (**Figure 1**) is a potent opiate analgesics, which has been employed in the treatment of a variety of medical conditions [1]. Pethidine hydrochloride is also used as an illicit drug and therefore it is placed on the schedule II controlled substances list (drugs that have acceptable medical use and have high potential for abuse) in the United States and many other countries. Pethidine is also prescribed as a substitute for heroin [2], and often used medically as postoperative analgesia. In sports, athletes often take far higher doses of drugs than have been given for therapeutic use or in clinical studies to excel in competition. They have been barred to use by the International Olympic Committee and other sports organizations [3]. Therefore, determination of pethidine has important practical meanings. Many Several sophisticated analytical methods were reported to determine the pethidine such as high performance liquid chromatography (HPLC) [4,5], gas chromatography [6], gas chromatography in

combination with mass spectrometry (GC-MS) [7,8], spectrophotometry [9] and potentiometric analysis [10-14]. Many of these methods involve several time-consuming manipulations, extraction steps, derivatization reactions that are liable to various interferences, and are not applicable to colored and turbid solutions either.

Potentiometric methods with ion-selective electrodes (ISE's) have proved to be effective for the analysis of pharmaceutical formulations and biological samples, because these sensors offer the advantages of simple design, construction, and manipulation, reasonable selectivity, fast response time, applicability to colored and turbid solutions and possible interfacing with automated and computerized systems. [15-17]. A number of ISEs based on PVC membrane [10-14], for determination of pethidine have been reported. However, these electrodes still have certain inherent limitations. Cleary, there is an urgent need for a recipe that would make the fabrication and optimization of potentiometric sensors with low detection limit, high stability and reproducibility a straightforward process.

The advantages of carbon paste electrodes, such as che-
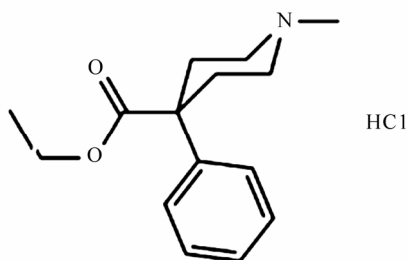
Figure 1. Chemical structure of pethidine hydrochloride.

mical inertness, robustness, low cost, renewability, very low background current, stable response, low ohmic resistance and no need for internal solution over conventional polymeric membrane electrodes has attracted the attention of researchers in recent years [15-18]. After careful review of literature, there is no report on determination of pethidine hydrochloride using a carbon paste electrode.

This paper describes the construction, potentiometric characterization, and analytical application of a pethidine-chemically modified carbon paste electrode (D-CMCPE) based on the use of pethidine-phosphotungstate (PD-PT) as electroactive materials and 2-nitrophenyl octyl ether (2-NPOE) as plasticizer. The results presented in this paper show that the sensor constructed for pethidine ion has a wide concentration range, low limit of detection, good Nernstain slope, and high selectivity over a wide variety of other cations and compared with electrodes previously reported [10-14].

2. Experimental

2.1. Reagents and Solutions

Pethidine hydrochloride PDCl was obtained from general administration of pharmacy, ministry of health (Gaza-Palestine). Graphite powder, 2-nitrophenyl octyl ether (2-NPOE), dioctyl phthalate (DOP), dibutyl phthalate (DBP), tris(2-ethylhexyl) phosphate (DOPh), dioctyl sebacate (DOS), tributyl phosphate (TPh), tricresyl phosphate (TCP) and dibutyl butyl phosphonate (DDBP), as well as metal salts were purchased from Aldrich and used as received. Silicotungstic acid (STA), phosphotungstic acid (PTA), phosphomolybdic acid (PMA), silicomolybdic acid (SMA) and sodium tetraphenyl borate (Na-TPB) were obtained from Sigma.

2.2. Apparatus

Potentiometric measurements were carried out with a digital millivoltmeter (SR-MUL-3800). pH measurements were made on a digital pH meter (Wissenscha-ftlich-Te-

chnische WerkstattenGmbH (WTW)-Germany) at room temperature ($25.0°C \pm 1.0°C$).

2.3. Preparation of Ion-Exchanger Complex

An ion-exchanger complex was made from pethidine hydrochloride (PD) and one of the following substances: silicotungstic acid (STA), silicomolybdic acid (SMA) phosphotungstic acid (PTA), phosphomolybdic acid (PMA), or sodium tetraphenyl borate (Na-TPB) according to a previously reported method [19]. This precipitated ion-pair was washed, dried and used as the active substances for preparing the chemically modified carbon paste electrodes of pethidine hydrochloride.

2.4. Preparation of the Electrode

A Teflon holder (12 cm length) with a hole at one end (7 mm diameter, 3.5 mm deep) for the carbon paste filling served as the electrode body. Electrical contact was made with a stainless steel rod through the centre of the holder. This rod moved up and down by screw movement to press the paste down when renewal of the electrode surface was needed. Modified carbon paste was prepared by mixing weighed amounts of PD-PT and high purity graphite. The mixture was homogenized, and then the impregnated carbon powder was added to a weighed amount of 2-nitrophenyl octyl ether (2-NPOE). A very high degree of homogenization is then achieved by careful mixing with a glass rod in an agate mortar and subsequent thorough crushing with a pestle. The ready-prepared paste was then packed into the hole of the electrode body. The carbon paste was smoothed onto paper until it had a shiny appearance and was used directly for potentiometric measurements without preconditioning requirements.

2.5. Sample Analysis

The standard addition method in which small increments (10 - 100 µl) of (0.1 M) TDCl solution were added to 50 mL aliquot-samples of various concentrations (5.0×10^{-6} to 1.0×10^{-5} M) PDCl was applied. The potential after each increment was recorded at $25°C \pm 0.1°C$ and used to calculate the concentration of TDCl in the drug samples.

The potentiometric titration of different volumes of 1.0×10^{-3} M and 1.0×10^{-2} M PDCl solution: 5 - 10 mL equivalent to 1.42 - 28.4 mg, were transferred to a 25 mL beaker, and titrated with a standard solutions of Na-TPB and PTA using the prepared PD-electrode as indicator electrode. The end points were determined from the S-shaped curve.

In the calibration graph method, different amounts of

PDCl were added to 50 mL of water comprising a concentration range from 1.0×10^{-7} to 1.0×10^{-2} M and the measured potential was recorded using the present electrode. Data were plotted as potential versus logarithm of the PD$^+$ activity and the resulting graph was used for subsequent determination of unknown drug concentration [20].

2.6. Analysis of Spiked Urine Samples

The samples (5ml of urine) were spiked with pethidine hydrochloride and left stirred for 5 min, transferred to a 25 mL volumetric flask and completed to the mark with distilled water to give 5.0×10^{-6} to 1.0×10^{-5} M PDCl. These solutions were subjected to the standard additions method or the calibration graph method for PDCl determination [21].

3. Result and Discussion

3.1. Characteristics of the Electrode

The general characteristics of sensor are outlined by determining its sensitivity, detection limit, linear range and selectivity coefficients. Some important features of carbon paste electrode, such as the properties of the plasticizer, the graphite (G)/plasticizer (P) ratio, the nature and amount of the ion-exchanger complex, are reported to significantly influence the sensitivity and selectivity of the sensor.

3.1.1. Effect of Ion-Exchanger
Ion-exchanger complex used in ISEs should have rapid exchange kinetics and adequate formation constants in the paste. In addition, they should have good solubility in the paste matrix and sufficient lipophilicity to prevent leaching from the paste into the sample solution [22,23]. The ion-exchangers of PD-ST, PD-SM, PD-PT, PD-PM and PD-TPB were prepared and tested as modifiers for the present electrode. The influences of the amount of the different pethidine ion-exchangers in the carbon paste were investigated and the corresponding results are summarized in **Table 1**. As can be seen, the electrode containing zero percentage of ion-exchanger complexes (sensor No. 1) showed a negligible response towards pethidine cations, whereas in the presence of the Ion-exchanger complexes the sensor displayed remarkable selectivity for pethidine cations, as found for electrode (composition #2) that contains PD-PT and produced the widest concentration range, the lowest detection limit and shortest response time with Nernstain slope towards PD$^+$ cations. The other ion-exchangers gave inferior response. Further increase in the ratio of the

ion-exchanger complexes (sensors No. 3 and 4), however, resulted in a little decrease in the response of the electrode, most probably due to some inhomogenieties and possible saturation of the paste [24].

3.1.2. Effect of Graphite/Plasticizer (G/P) Ratio
Different graphite/plasticizer ratios that is 0.85, 0.95, 1.05, 1.15 and 1.30 using 2-NPOE as plasticizer while keeping the amount of ion-exchanger complex constant (*i.e.* 0.5%) were examined while optimizing the membrane composition as shown in **Table 1**. The paste with (G/P) ratio of 0.95 showed the optimum physical properties and ensured high enough mobilities of their constituents [25] and was found to give the best reproducibility and sensitivity of 54.2 mV per decade over the widest linear concentration range of 2.1×10^{-6} - 1.0×10^{-2} M in comparison to the other ratios tested. Pastes with G/P more than 1.30 produced "crumbly" pastes and those with ratio smaller than 0.85 had a consistency resembling that of "peanut butter", *i.e.*, not workable.
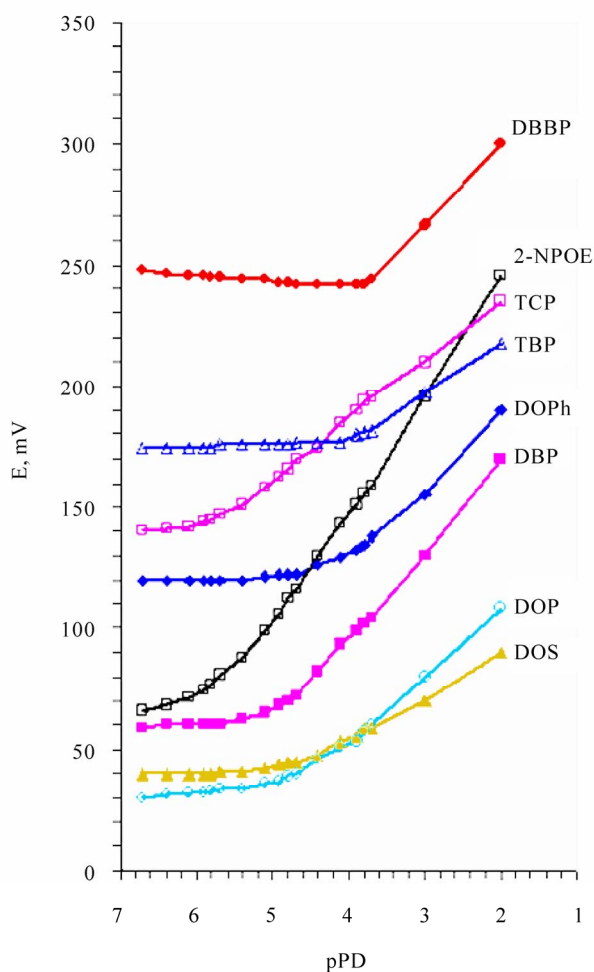
3.1.3. Effect of Plasticizers
Two parameters are of importance when manufacturing a carbon paste: 1) its mechanical stability and 2) its active surface area. Mechanical stability can be interpreted as the ability of the carbon paste to avoid erosion in solution. The use of plasticizers will give some permeable properties to the paste and will improve its mechanical stability by promoting binding between grains [26]. In addition, the solvent mediator, in particular, has a dual function: it acts as a liquifying agent, enabling homogenous solubilization and modifying the distribution constant of the ion-exchanger complex used. The proportion of solvent mediator must be optimized in order to minimize the electrical asymmetry of the paste, to keep the sensor as clean as possible, and to stop leaching to the aqueous phase [27]. In exploration for a suitable plasticizer for constructing this electrode, we used seven plasticizers, with the values of dielectric constants, lipophilicity and molecular weight respectively listed in parantheses, namely, 2-NPOE ($\varepsilon r = 23.6$, $P_{TLC} = 5.9$, M.wt. = 251), DOP ($\varepsilon r = 5.1$, $P_{TLC} = 7.0$, M.wt. = 391), DBP ($\varepsilon r = 6.4$, $P_{TLC} = 4.5$, M.wt. = 278), DOS ($\varepsilon r = 3.9$, $P_{TLC} = 10.1$, M.wt. = 427), DOPh ($\varepsilon r = 4.8$, $P_{TLC} = 10.2$, M.wt. = 434), TBP ($\varepsilon r = 8.0$, $P_{TLC} = 4.0$, M.wt. = 266), TCP ($\varepsilon r = 6.9$, M.wt. = 368) and DBBP ($\varepsilon r = 4.6$, M.wt = 250) in sample electrodes to figure out the plasticizer with the best response. The sensor with 2-NPOE as a solvent mediator produced the best response, as shown in **Figure 2**, likely due to better dielectric characteristics of 2-NPOE comparing to other solvents, and the ability of 2-NPOE to extract pethidine ions from the aqueous solution to the organic paste phase [28].

Table 1. Optimization of paste ingredients of the pethidine sensor.

Sensor	Composition (%)			Electrode response			
	I-E	G	P (2-NPOE)	S	C.R.	LOD	$R_{(s)}$
PD-PT							
1-	--	51.5	48.5	40.8	1.7×10^{-4} - 1.0×10^{-2}	8.3×10^{-5}	20 - 25
2-	0.5	48.5	51.0	54.2	2.1×10^{-6} - 1.0×10^{-2}	7.3×10^{-7}	5 - 8
3-	1.0	48.2	50.8	50.9	5.3×10^{-6} - 1.0×10^{-2}	3.0×10^{-6}	8 - 12
4-	2.0	47.8	50.2	48.2	5.7×10^{-6} - 1.0×10^{-2}	4.2×10^{-6}	10 - 12
PD-PM							
5-	0.5	48.5	51.0	48.3	6.6×10^{-5} - 1.0×10^{-2}	2.3×10^{-5}	13 - 15
6-	1.0	48.2	50.8	48.5	7.9×10^{-5} - 1.0×10^{-2}	3.9×10^{-5}	20 - 23
7-	2.0	47.8	50.2	47.1	9.2×10^{-5} - 1.0×10^{-2}	5.3×10^{-5}	17 - 20
PD-ST							
8-	0.5	48.5	51.0	47.1	5.2×10^{-6} - 1.0×10^{-2}	3.3×10^{-6}	10 - 13
9-	1.0	48.2	50.8	46.5	8.5×10^{-6} - 1.0×10^{-2}	5.1×10^{-6}	12 - 15
10-	2.0	47.8	50.2	46.2	9.4×10^{-5} - 1.0×10^{-2}	5.5×10^{-6}	15 - 18
PD-SM							
11-	0.5	48.5	51.0	51.5	3.6×10^{-5} - 1.0×10^{-2}	2.3×10^{-5}	12 - 15
12-	1.0	48.2	50.8	49.6	5.9×10^{-5} - 1.0×10^{-2}	3.7×10^{-5}	15 - 20
13-	2.0	47.8	50.2	49.0	7.8×10^{-5} - 1.0×10^{-2}	4.3×10^{-5}	20 - 23
PD-TPB							
14-	0.5	48.5	51.0	49.2	2.6×10^{-5} - 1.0×10^{-2}	1.3×10^{-5}	15 - 20
15-	1.0	48.2	50.8	47.1	3.2×10^{-5} - 1.0×10^{-2}	1.7×10^{-5}	12 - 15
16-	2.0	47.8	50.2	47.7	3.8×10^{-5} - 1.0×10^{-2}	2.0×10^{-5}	15 - 18
PD-PT with different plasticizers							
plasticizers							
(2-NPOE)	0.5	48.5	51.0	54.2	2.1×10^{-6} - 1.0×10^{-2}	7.3×10^{-7}	5 - 8
(DOP)	0.5	48.5	51.0	46.5	8.1×10^{-5} - 1.0×10^{-2}	5.5×10^{-6}	12 - 15
(DBP)	0.5	48.5	51.0	50.6	3.2×10^{-5} - 1.0×10^{-2}	1.0×10^{-5}	15 - 18
(DOS)	0.5	48.5	51.0	42.6	5.5×10^{-5} - 1.0×10^{-2}	3.2×10^{-5}	13 - 17
(DOPh)	0.5	48.5	51.0	51.2	8.3×10^{-6} - 1.0×10^{-2}	6.5×10^{-6}	15 - 20
(TCP)	0.5	48.5	51.0	52.6	5.3×10^{-6} - 1.0×10^{-2}	2.5×10^{-6}	10 - 12
(TBP)	0.5	48.5	51.0	41.3	2.1×10^{-4} - 1.0×10^{-2}	1.7×10^{-4}	20 - 23
(DBBP)	0.5	48.5	51.0	40.9	1.8×10^{-4} - 1.0×10^{-2}	1.0×10^{-4}	20 - 25
PD-PT with different g/p ratios							
g/p ratios							
0.85	0.5	45.7	53.8 (2-NPOE)	52.8	2.5×10^{-6} - 1.0×10^{-2}	8.7×10^{-7}	8 - 10
0.95	0.5	48.5	51.0 (2-NPOE)	54.2	2.1×10^{-6} - 1.0×10^{-2}	7.3×10^{-7}	5 - 8
1.05	0.5	51.0	48.5(2-NPOE)	53.8	2.7×10^{-6} - 1.0×10^{-2}	8.1×10^{-7}	10 - 12
1.15	0.5	53.2	46.3 (2-NPOE)	51.8	3.2×10^{-6} - 1.0×10^{-2}	1.3×10^{-6}	10 - 12
1.30	0.5	56.2	43.3 (2-NPOE)	48.9	7.3×10^{-6} - 1.0×10^{-2}	4.4×10^{-6}	12 - 15

I. E: ion-exchanger complex, G: graphite, P: plasticizers, S: slope (mV/decade), C.R.: concentration range (M), LOD: limit of detection, R (s): response time (s).

Figure 2. Effect of different plasticizers on the response of PD-CMCPE.

Among the different compositions studied, a paste containing ion-exchanger complex 0.5 wt% PD-PT, 48.5 wt% graphite, 51.0 wt% 2-NPOE exhibited the best response characteristics and the lowest detection limit. Therefore, this composition was used to study various operation parameters of the electrodes. The electrochemical performance characteristics of this electrode were systematically evaluated according to the IUPAC recommendations [29].

3.2. Surface-Renewal and Reproducibility of the Electrode

The main attraction of using the modified electrode is that the electrode surface can be renewed after every use. The bulk modified electrode can be renewed by squeezing a little carbon paste out of the tube and a fresh surface is smoothed on a piece of weighing paper whenever needed [30]. Accordingly, a paste of optimum composi-

tion and suitable weight (1.5 g) can be used for several months without any deterioration or change in the response of the electrode. The slope of the calibration graph was found to decrease slightly from 54.4 to 50.8 mV/decade after three times of use. This decrease may be attributed to memory effect due to the surface contamination [31]. In this case, the electrode surface should be renewed. The repeatability of the potential reading of the electrode was examined by subsequent measurements of 1×10^{-4} M PDCl solution immediately after measuring the first set of solutions at 1.0×10^{-3} M PDCl. The standard deviation of measuring emf for 5 replicate measurements was found to be 1.127 for 1.0×10^{-4} M solution and 0.747 for 1.0×10^{-3} M solution.

3.3. Response Time and Reversibility of the Electrode

For analytical applications, dynamic response time is a significant parameter for any sensor. The response time of the electrode is defined as the time between addition of the analyte to the sample solution and the time when a limiting potential has been reached [29].

In this work, the response time of the electrode was measured by varying the pethidine concentration over the range 1.0×10^{-5} to 1.0×10^{-2} M. The electrode reaches equilibrium in about 5 - 8 s. As shown in **Figure 3**. To evaluate the reversibility of the electrode, the potential measurements were performed in the sequence high-to-low (from 1.0×10^{-2} to 1.0×10^{-5} M) sample concentrations. **Figure 3** showed that the response of the electrode was reversible; although the time needed to reach equilibrium values (12 s) was longer than that for low-to-high sample concentrations.

3.4. Effect of Diverse Ions

The separate solution method (SSM) is recommended by IUPAC to determine the selectivity coefficient of the ISE [32]. SSM is based on Nickolsky-Eisenman equation. However, it has been shown that this method suffers some limitations in terms of the values for ions of unequal charges, a non-Nernstain behavior of interfering ions [33]. Therefore another method named the "matched potential method (MPM)" was recommended [32] especially when the primary ion and/or the interfering ion dissatisfy with the Nernst response or when the involved ions have unequal charges [34]. The resulting values, presented in **Table 2**, show that the electrode display significantly high selectivity for pethidine over many common organic and inorganic compounds, drugs, sugars, amino acids as well as some anions. In pharmaceutical analysis, it is important to test the selectivity towards
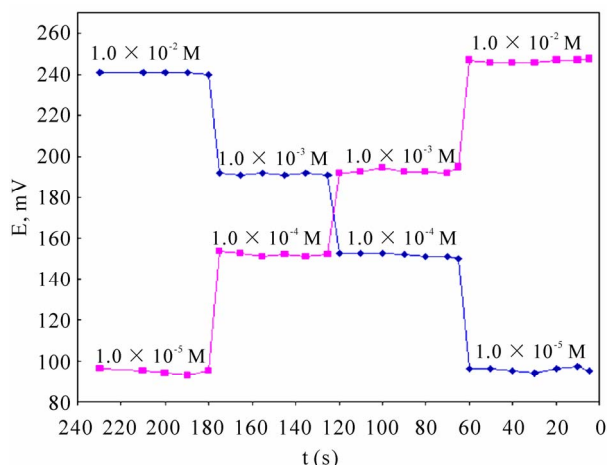
Figure 3. Dynamic response of sensor A for step changes in concentration of pethidine hydrochloride (from low to high and vice versa).

Table 2. Selectivity coefficients of various interfering ions for PD-CMCPE.

Interfering ions	SSM	MPM
NH^+	1.41×10^{-4}	8.41×10^{-5}
Na^+	9.52×10^{-5}	1.18×10^{-5}
K^+	2.71×10^{-4}	1.20×10^{-4}
Li^+	4.34×10^{-4}	1.66×10^{-4}
Cd^{2+}	5.69×10^{-4}	8.34×10^{-6}
Mg^{2+}	1.94×10^{-4}	7.81×10^{-6}
Ca^{2+}	1.13×10^{-4}	2.10×10^{-5}
Ba^{2+}	8.02×10^{-4}	2.02×10^{-5}
Zn^{2+}	2.73×10^{-4}	5.11×10^{-5}
Co^{2+}	1.19×10^{-4}	3.85×10^{-5}
Al^{3+}	6.98×10^{-4}	7.73×10^{-5}
Ce^{3+}	1.86×10^{-4}	4.30×10^{-5}
Diclofenac sodium	2.53×10^{-2}	4.86×10^{-2}
Spiramycine	3.41×10^{-2}	4.86×10^{-2}
Spectinomycine Hcl	2.93×10^{-2}	2.47×10^{-2}
Captopril	6.76×10^{-2}	2.45×10^{-2}
Ephidrine	1.27×10^{-2}	8.89×10^{-3}
Lidocaine	1.27×10^{-1}	4.86×10^{-2}
D-Fractose	-	9.14×10^{-7}
D- Galactose	-	1.35×10^{-6}
Maltose	-	5.54×10^{-6}
Sucrose	-	8.04×10^{-6}
Glucose	-	2.47×10^{-6}

the excipients such as such as lactose, glucose, sucrose, starch, stearic acid, magnesium stearate and microcrystalline cellulose and the fillers added to the pharmaceutical preparations. The interference of some of these excipients was explored and measured. It is found that they cause minor effect on the function of the electrode as shown in **Table 2**.

3.5. Effect of Temperature

To study the thermal stability of the sensor, calibration graphs were constructed at different test solution temperatures 20, 30, 40, 50 and 60°C. From these graphs the electrode potentials at pPD = 0 were obtained and plotted versus (t−25), where t is the temperature of the experiment. A straight line plot was obtained for each electrode with slope represents the thermal coefficient value (dE/dt) of the electrode [35]. The value (dE/dt) of the electrode was found to be 0.00071 V/°C. This indicates fairly high thermal stability of the electrode within the investigated temperature range and shows no deviation from the theoretical Nernstian behavior.

3.6. Effect of pH

The pH dependence of the potentials of the proposed electrode was tested over the pH range 2.2 - 10.0 for 1.0×10^{-5} and 1.0×10^{-4} M PDCl solutions. The acidity was adjusted by adding small volumes of (1.0 M HCl or NaOH) to the test solutions and the variation in potential was followed. As it can be seen in **Figure 4**, the potential response remains almost constant over the pH range 2.7 - 6.8 which can be taken as the working pH range of the electrode. However, there is a slight deviation at pH values lower than 2.7 which may be due to H^+ interference. On the other hand, the potential decreases gradually at pH values higher than 6.8. This drop may be attributed to formation of free pethidine base in the test solution.

4. Applications

4.1. Titration of Pethidine Solution with a Standard PTA and Na-TPB Solution

The PD-CMCPE was successfully used as an indicator electrode in the potentiometric titration of 5 ml of 0.01 M (14.2 mg) of pethidine hydrochloride with a standard solution of Na-TPB and PTA solution. The method for pethidine ion (PD) titration is based on the decrease of (PD) concentration by precipitation with PTA and Na-TPB standard solution. As is obvious from **Figure 5**,
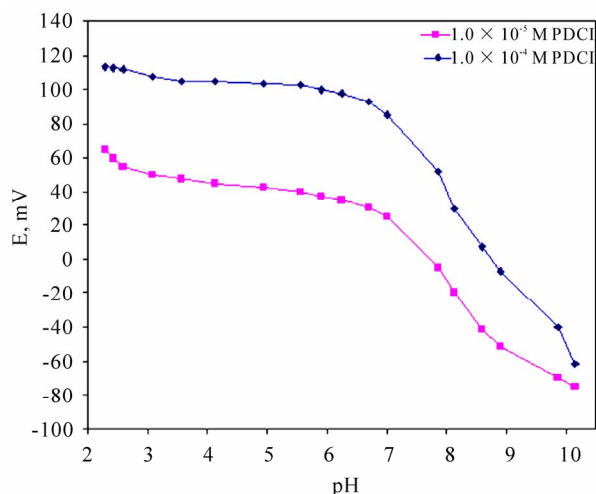
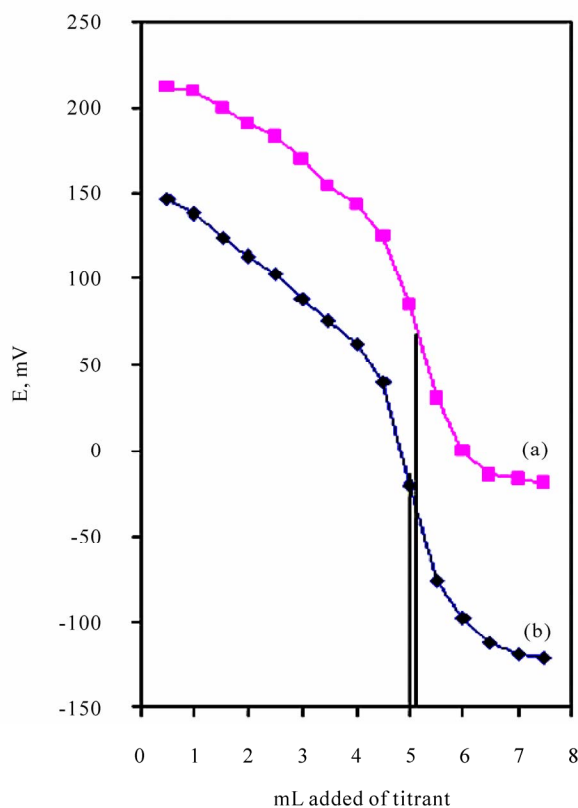**Figure 4. Effect of pH of the test solution on the potential response of PD-CMCPE.**

Figure 5. Potentiometric titration of 14.2 mg PDCl with Na-TPB (a) and PTA (b) as titrants using PD-CMCPE.

the amount of pethidine can be accurately determined from the end point of the titration curve.

4.2. Determination of Pethidine in Ampoules

The standard additions and calibration methods were applied for determination PDCl content in ampoule samples as can be seen in **Table 3**, the recovery of PDCl is almost quantitative.

4.3. Recovery and Determination of Pethidine Ions in Urine

Recovery experiments were conducted by spiking urine samples with appropriate amounts of pethidine ions, and determined by this electrode using the standard addition method and calibration curve. The results shown in **Table 3**. Recoveries and R.S.D. values range between 96.6% and 103.0% of pethidine, and 0.27 to 1.33, respectively. It is noted that accurate and reproducible results Thus the sensor can be employed for quantification of pethidine in urine samples.

5. Comparison of the Pethidine Selective Electrodes

The performance characteristics of the proposed electrode and those of some reported carbon paste electrodes are presented in **Table 4** for comparison. It is clear that the proposed electrode is comparable with most of the reported electrodes with regard to working concentration range, response time and low detection limit. Overall evaluation indicates this electrode is more useful in such applications.

6. Conclusions

The proposed chemically modified carbon paste electrode based on pethidine phosphotungstate as an electroactive ion exchanger complex might be a useful analytical tool and interesting alternative for the determination of PD ions in pharmaceutical preparations and urine samples. The electrode shows high sensitivity, reasonable selectivity, fast static response, long term stability and applicability over a wide concentration range with minimal sample pretreatment. The electrode developed is superior as compared with the pethidine selective electrode described in the literature [10-14].

7. Acknowledgements

Table 3. Results for determination of PDCl in ampoules and urine samples using PD-CMCPE.

Sample	Method*	PD/mg[a]	Recovery %	RSD[b] %	Standard error
Ampoule					
	SDM	0.0248	96.8	0.85	0.025
		0.248	97.8	0.48	0.032
	CCM	0.0355	101.5	0.35	0.054
		0.355	100.8	0.27	0.033
Urine					
	SDM	0.0248	96.6	0.74	0.021
		0.248	97.8	1.02	0.017
	CCM	0.0355	101.5	1.33	0.051
		0.355	100.8	1.08	0.041
PTM using Na-TPB and PTA as a titrant					
Na-TPB		1.42	100.5	0.72	0.026
		14.2	100.0	0.29	0.022
PTA		1.42	101.2	0.36	0.019
		14.2	103.0	0.44	0.047

[a]Milligrams taken of PDCl in ampoules or spiked to urine samples, [b]Average of three determinations, Methods* (used in analytical applications) SDM: standard additions method, CCM: calibration curve method, PTM: potentiometric titration method.

Table 4. Comparison of the proposed pethidine sensor with published sensors.

Reference	S	C. R	LOD	$R_{(s)}$
[10]	55.3	1.0×10^{-5} - 1.0×10^{-2}	3.3×10^{-6}	10
[11]	53.7	1.0×10^{-5} - 1.0×10^{-2}	9.9×10^{-7}	< 30
[12]	51.8	1.0×10^{-5} - 1.0×10^{-2}	2.2×10^{-6}	< 30
[13]	56.7	5.0×10^{-6} - 1.0×10^{-2}	8.2×10^{-7}	< 30
[14]	53.5	1.0×10^{-5} - 1.0×10^{-3}	4.4×10^{-6}	30
Present work	54.2	2.1×10^{-6} - 1.0×10^{-2}	7.3×10^{-7}	5 - 8

C.R.: concentration range (M), LOD: limit of detection, S: slope (mV/decade), $R_{(s)}$: response time.

for encouragement, support and providing facilities for research.

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