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Chemically modified carbon paste electrode for the potentiometric flow injection analysis of piribedil in pharmaceutical preparation and urine

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Abstract

A new carbon paste electrode selective for piribedil (PD) was prepared and fully characterized in terms of composition, usable pH range, response time and thermal stability. The electrode active recognition is by liquid ion-exchange mechanism via the use of piribedil phosphomolybdate as ion-exchanger dissolved in tricresyl phosphate as a more suitable solvent mediator for the paste. The modified electrode showed a Nernstian slope of 58.4 ± 0.6 mV over the concentration range of 7.5×10^{-7} to 1×10^{-3} M with an average recovery of 98.3–101.0% and R.S.D. of 0.45–1.31%. The electrode exhibits good selectivity for PD with respect to a large number of inorganic cations, organic cations, sugars and amino acids. The developed electrode was successfully used for the potentiometric determination of PD in its aqueous solutions, pharmaceutical preparation, and urine in batch and flow injection analysis (FIA).

Keywords: Piribedil; Chemically modified carbon paste electrode; Ion-exchanger; Flow injection analysis

1. Introduction

Chemically modified carbon paste electrodes (CMCPEs) have been successfully applied as potentiometric sensors for determination of various species [1]. Most of these electrodes are based on the ion-exchange mechanism of the active component incorporated into the carbon paste matrix. These electrodes offer very attractive properties for the electrochemical investigation of various inorganic and organic species.

In comparison with ion-selective electrodes based on polymeric membranes, CMCPEs possess the advantages of ease of preparation, ease of regeneration, and very stable response in addition to the very low Ohmic resistance [2,3], probably due to the formation of very thin film of pasting liquid coated onto small particles of carbon powder [4,5]. Therefore, CMCPEs have found direct application in a variety of analytical situations, such as amperometry [6–9] and voltammetry [10,11], in addition to potentiometry [12,13].

Piribedil (PD) is an alkoxybenzyl-4-(2-pyrimidinyl) piperazine derivative with vasodility activity [14]. Piribedil is a dopamine agonist acting on D2 and D3 central nervous system dopamine receptors [15]. The drug has proved active in patients with parkinson's diseases, particularly in the control of tremors [16].

The reported methods for the determination of piribedil are mainly chromatographic. They include gas chromatography with nitrogen sensitive detector [17] or combined with mass spectrometry [18], HPLC [19] and micellar electrokinetic capillary chromatography [20]. In spite of the high sensitivities of these chromatographic methods, they are very expensive; involve the use of complex procedures with several sample manipulations, and require long analysis time. Besides, none of them are easy to automate. The spectrophotometric methods described for the analysis of piribedil [21,22] may have good accuracy and precision but they are usually suffer from poor selectivity. Electrochemical investigation of piribedil by differential pulse and square wave voltammetry was described [23].

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Potentiometric methods with CMCPEs can provide valuable and straightforward means of assaying PD in complex mixtures, as they make possible the direct determination of ions in solutions with high selectivity. To the best of our knowledge, there are only two reports on the use of plastic membrane potentiometric sensors for the determination of PD based on tetraphenylborate [24] and Bi(III)-iodide [25] with detection limits of 1×10^{-5} and 2×10^{-5} M, respectively. These electrodes lack good stability, sufficient selectivity and suffer from limited concentration ranges. It was, therefore, felt worthwhile to develop a better sensor for PD using CMCPE facilities.

Previous work from this laboratory described the use of the highly insoluble ion-associates formed from the reactions of heteropoly acids (silicotungstic, silicomolybdic, phosphotungstic and phosphomolybdic) with some organic cations as sensory molecules for a group of ion-selective electrodes [26,27].

In this work, the preparation of a carbon paste electrode, namely PD-CMCPE, modified with piribedil-phosphomolybdate is described. The investigation of the optimized composition of the paste and the experimental variables that contribute to the electrode response led to the development of a simple, selective, and reliable method for PD determination. Studies on the determination of PD in pharmaceutical preparation (tablets dosage) and in spiked urine samples were carried out to illustrate the feasibility of the proposed method in both batch and FIA conditions.

2. Experimental

2.1. Reagents and solutions

Piribedil was kindly provided from Servier Egypt Industries, under license of Les Laboratories Servier, France. Stock PD solution of about 0.01 M was prepared by dissolving 0.3 g of the compound in 4 mL 0.5 M HCl, and diluting with water to 100 mL. The exact concentration of PD solution was determined spectrophotometrically using 2,3-dichloro-5,6-dicyano-*p*-benzoquinone reagent [22]. The pharmaceutical preparation containing PD, Trivastal® (tablets dosage, 20 mg/tablet) was obtained from local drug stores. Graphite powder, dibutyl phthalate (DBP), dioctyl phthalate (DOP), dioctyl sebacate (DOS), tricresyl phosphate (TCP), diisononyl phthalate (DINP) were used as received from Aldrich. Aqueous solutions of silicotungstic acid (STA), silicomolybdic acid (SMA), phosphotungstic acid (PTA) and phosphomolybdic acid (PMA) were prepared from materials of analytical grade purity. Doubly distilled water was used throughout.

2.2. Preparation of ion-exchangers

The ion-exchangers piribedil silicotungstate (PD-ST), piribedil silicomolybdate (PD-SM), piribedil phosphotungstate (PD-PT) and piribedil phosphmolybdate (PD-PM) were prepared as previously described by Ibrahim [27]. The chemical compositions of these compounds were found to be PD_4ST, PD_4SM, PD_3PT, and PD_3PM as confirmed by (C, H and N) elemental analysis using automatic CHN analyzer (Perkin-Elmer model 2400). The metal content in each ion-exchanger was determined by digesting the compound in boiling H_2SO_4/H_2O_2 mixture [28] followed by atomic absorption assay using Perkin-Elmer spectrometer (model 2380).

2.3. 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 center of the holder. This rod can move 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 0.025–0.10 g of the ion-exchanger and 0.20 g high purity graphite with acetone. The mixture was homogenized, left at room temperature to evaporate acetone, and then the impregnated carbon powder was added to 0.160–0.275 g of tricresyl phosphate. Very intimate homogenization is then achieved by careful mixing with glass rod in an agate mortar and afterwards rubbed by intensive pressing with a pestle. The ready-prepared paste is 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. After several times of use, a fresh electrode surface was obtained by squeezing out a small amount of the paste, scrapping off the excess against a conventional paper and polishing the electrode on a smooth paper to obtain a shiny appearance again.

2.4. Apparatus

The potentiometric measurements in steady state mode were carried out with a Jenway 3010 digital pH/mV meter. A Techne circulator thermostat Model C-100 (Cambridge, England) was used to control the temperature of the test solution. A WTW (Water Treatment Warehouse, Inc.) packed saturated calomel electrode (SCE) was used as an external reference electrode. The electrochemical system is represented as follows:

PD-CMCPE/test solution//SCE.

A single-stream flow injection manifold (Fig. 1) was used. It is composed of a four channel peristaltic pump (Ismatec, ISM 827, Zurich, Switzerland) and an injection valve model 5020 with exchangeable sample loop from Rheodyne (Cotati CA, USA). The electrode was connected to a WTW micro-processor pH/ion-meter pMX 2000 (Weilheim, Germany) and interfaced to a strip chart recorder model BD111 from Kipp and Zonn (Deflt, Netherlands). In this flow system,

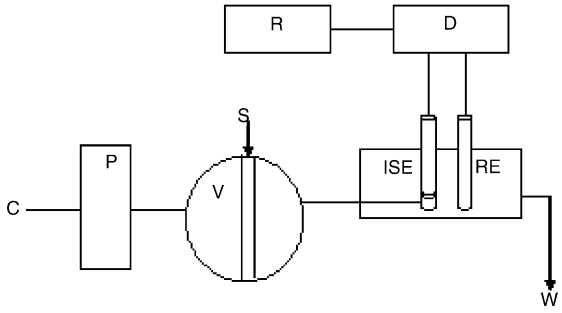

Fig. 1. Single-stream FIA manifold for PD determination (C, carrier stream; S, sample; P, peristaltic pump; V, injection valve; ISE, PD-electrode; RE, reference electrode; D, detector; R, recorder; W, waste).

a wall-jet cell, providing low dead volume, fast response, good wash characteristics, ease of construction and compatibility with electrodes of various shapes and sizes, was used where a homemade Teflon-cup with axially positioned inlet polypropylene tubing is mounted at the sensing surface of the electrode body. The optimized distance between nozzle and the sensing surface of the electrode was 5 mm; this provides the minimum thickness of the diffusion layer and consequently, a fast response.

2.5. Potentiometric determination of PD

The standard additions method [29] was applied in which small increments (50–100 μL) of standard PD solution (10^{-1} M) were added to 50 mL aliquot samples of various concentrations from the drug sample solution equivalent to 0.298–59.66 mg PD. The change in potential at ($25.0 \pm 0.1\,^{\circ}$C) was recorded for each increment and these data were used to calculate the concentration of PD in the sample solution.

2.6. Determination of PD in Trivastal tablets

The contents of 15 tablets (20 mg PD/tablet) of Trivastal® were powdered and an accurately weighed portion equivalent to 200 mg PD was dissolved in 100 ml distilled water according to the method of British Pharmacopoeia [30]. Different volumes of the solution (1.0–10.0 mL) were taken and subjected to potentiometric determination applying the standard additions method.

2.7. Determination of PD in urine

Different quantities of PD and 5 mL urine were transferred to a 100 mL volumetric flask and completed to the mark with 10^{-4} M HCl to give solutions of pH ranging from 3.5 to 6.0 (the optimum pH range of the electrode performance) and 1×10^{-4} to 2.5×10^{-3} M with respect to PD. The PD content in each sample was recovered by the potentiometric standard additions method.

3. Results and discussion

3.1. Composition and characteristics of the electrode

In preliminary experiments, carbon pastes with and without ion-exchangers were prepared. The pastes with no exchangers displayed no measurable response toward PD^+ ions, whereas, in the presence of the proposed ion-exchangers, the optimized sensors demonstrated an appreciable response and remarkable selectivity for PD^+ over several common inorganic and organic cations. It is well known that the selectivity, linear dynamic range and sensitivity obtained for a given CMCPE depends significantly on the paste composition [31], the nature of the solvent mediator [1,31] and any additives used [32].

The influence of the plasticizer type and concentration on the characteristics of the PD-sensor was investigated by using five plasticizers with different polarities including DBP, DOP, DOS, TCP, and DINP. As is quite obvious from emf-pPD plots (Fig. 2), the use of TCP results in a Nernstian linear plot over a wide concentration range, whereas in the case of other solvent mediators, the slopes of the potentiometric response are much different from the expected Nernstian value of 59.5 mV/concentration decade, although at a limited concentration range. It seems that TCP, as a low polarity compound, provides more appropriate conditions for incorporation of the highly lipophile PD^+ ion into the paste prior to its exchange with the soft ion-exchanger.

Besides the critical role of the nature and the amount of plasticizer in preparing PD-CMCPE, the influence of the type

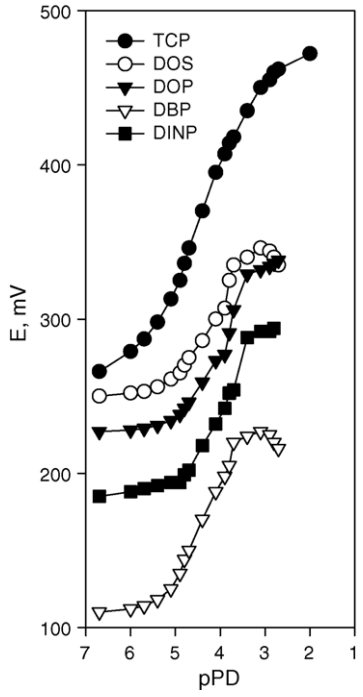

Fig. 2. Effect of different plasticizers on the potential response of PD-CMCPE.

Table 1
Optimization of paste ingredients

Number	Composition (%)				
	Graphite	TCP (P)	Ion-exchanger (I)	P/I ratio	Slope (mV/decade)
1	40	55	PD-ST, 5	11	22.3
2	40	50	PD-ST, 10	5	28.5
3	40	45	PD-ST, 15	3	35.1
4	40	40	PD-ST, 20	2	33.0
5	40	35	PD-ST, 25	1.4	30.4
6	40	55	PD-SM 5	11	25.4
7	40	50	PD-SM, 10	5	26.7
8	40	45	PD-SM, 15	3	26.1
9	40	40	PD-SM, 20	2	30.6
10	40	35	PD-SM, 25	1.4	23.0
11	40	55	PD-PT, 5	11	32.8
12	40	50	PD-PT, 10	5	36.4
13	40	45	PD-PT, 15	3	42.2
14	40	40	PD-PT, 20	2	45.9
15	40	35	PD-PT, 25	1.4	40.6
16	40	55	PD-PM, 5	11	41.1
17	40	50	PD-PM, 10	5	49.5
18	40	45	PD-PM, 15	3	55.3
19	40	40	PD-PM, 20	2	58.4
20	40	35	PD-PM, 25	1.4	54.5
21	40	32	PD-PM, 28	1.1	52.0

and amount of the ion-exchanger on the potential response of the electrode were investigated and the results are summarized in Table 1. As it is clear from this table, the electrodes modified by PD-ST, PD-SM, or PD-PT exhibit sub-Nernstian slopes not more than 46 mV/decade (numbers 1–15). The plasticizer/ion-exchanger ratio (P/I) of 2 displayed the best results for all electrodes. The calibration slope of the electrode modified by PD-PM increased with increasing ionophore content until a value of 20% is reached (number 19). However, further addition of PD-PM resulted in a diminished response slope of the electrode, most probably due to some inhomogenities of the pastes (numbers 20 and 21). The electrode number 19 (modified by 20% PD-PM with 40% TCP as plasticizer) was selected in this study and its electrochemical performance characteristics in both batch and FIA conditions were systematically evaluated according to the IUPAC recommendations [33], and summarized in Table 2.

The lower limit of detection (LOD) of the electrode in batch mode, defined as the concentration range of PD corresponding to the intersection of the two extrapolated linear segments of the calibration graph, equals to $1\ (\pm 0.1) \times 10^{-6}$ M. In flow analysis the LOD (or the minimum detectable value) is 7.3×10^{-7} M, which is the concentration derived from the smallest measurable net signal (R_{LOD}) that can be determined with reasonable certainty based on a statistical basis [34]. It is defined by the analyte concentration which yields a detector signal (R_{LOD}) equals to the background signal (R_{bg}) plus a multiple (k) of the standard deviation of the blank signal, s_B:

$$R_{LOD} = R_{bg} + ks_B$$

The limit of detection (limit of determination) in concentration units is given by:

$$C_{LOD} = \frac{ks_B}{S}$$

The multiple k depends on the adopted statistical significant level, and S is the sensitivity which is defined as the change in the detector signal (ΔR) divided by the change of concentration (ΔC).

The reproducibility of the PD-CMCPE was evaluated by preparing a series of five electrodes with similar paste

Table 2
Response characteristics of PD-CMCPE

Parameter	Batch	FIA
Electrode composition	20% PD-PM, 40% graphite and 40% TCP	
Slope (mV/decade)	58.4 ± 0.6	75.5 ± 1.0
Concentration range (M)	2.5×10^{-6} to 1.0×10^{-3}	7.5×10^{-7} to 1.0×10^{-3}
Lower detection limit (LOD) (M)	1.0×10^{-6}	7.3×10^{-7}
Limit of quantification (LOQ) (M)	2.5×10^{-6}	7.5×10^{-7}
R.S.D. (%) of intercepts	0.93	–
Working pH range	3.5–6.0	3.5–6.0
Response time (s)	≤7–10	≤3–5

composition (number 19) and the response of these electrodes to PD^+ ion concentration was tested. The results show that the average of slopes, detection limits and linear dynamic ranges were 58.4 ± 0.6 mV/decade, 1.0 (± 0.1) $\times 10^{-6}$ M and [2.5 (± 0.3) $\times 10^{-6}$ to 1.0 (± 0.5) $\times 10^{-3}$ M], respectively. The standard deviation of measurements of 1×10^{-5} M PD^+ solution with these five electrodes was 0.87.

The repeatability of the potential reading of the electrode was examined by subsequent measurements in 1×10^{-3} M PD solution immediately after measuring the first set of solutions at 1.0×10^{-4} M PD. The standard deviation for five replicate measurements of emf was found to be 1.31 in 1.0×10^{-4} M solution and 0.45 in 1.0×10^{-3} M solution. The slope of the calibration graph obtained by this electrode was found to decrease slightly after several times of use, which may be attributed to surface contaminations. In this case, a new surface was obtained as described in the experimental section.

3.2. Optimization of FIA response

The parameters of the flow injection system were optimized using 0.033 M Na_2SO_4 solution as a carrier stream in a low dispersion manifold. In order to stabilize the baseline, the carrier stream was adjusted to be 1×10^{-7} M with respect to PD.

The effect of flow rate on the response was verified using different flow rates (4.15–27 mL/min) for the same sample volume of 10^{-3} M PD solution. With a constant injection volume, the residence time of the sample is inversely proportional to the flow rate and the recovery time increases linearly with residence time of the sample at the active electrode surface [35]. It was found that, as the flow rate increased, the peaks become higher and narrower until a flow rate of 17.85 mL/min is reached, where the peaks obtained at higher flow rates are nearly the same. This flow rate was used through this work, providing approximately 99% of the maximum peak height obtained by higher flow rates, a shorter time to reach the baseline and less consumption of the carrier.

The sample volume affects the response of the electrode in a significant way. In general, the higher the sample volume, the higher peak heights and longer residence time at the electrode surface. This requires a longer time to reach the baseline and greater consumption of the sample [36]. Thus, the sample volume is very important to optimized to increase the sensitivity but without a significant decrease in the analytical accuracy. Samples with different volumes (9.4–500 μL) of 1.0×10^{-3} M PD where examined. The sample loop of size 150 μL was used throughout this work, giving approximately 95% of the maximum peak obtained by 500 μL loop, but with shorter time to reach the baseline and less consumption of samples.

3.3. Response time

The dynamic response time [33] of the electrode was tested by measuring the time required to achieve a steady state potential (within ±1 mV) after successive immersion of the electrode in a series of PD solutions, each having a 10-fold increase in concentration from 1.0×10^{-5} to 1.0×10^{-3} M. The electrode yielded steady potentials within 7–10 s. The potential reading stay constant, to within ±2 mV, for at least 15 min. The potential–time plot for the response of the electrode is shown in Fig. 3.

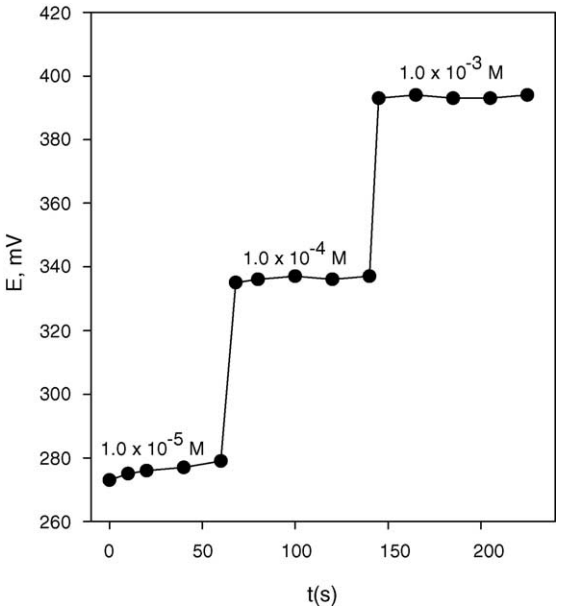

Fig. 3. The potential–time plot for the response of PD-CMCPE.

3.4. Effect of temperature

To study the thermal stability of the electrode, calibration plots [electrode potential ($E_{electrode}$) versus pPD] were constructed at different test solution temperatures covering the range 25–55 °C (Fig. 4). The standard cell potentials (E^0_{cell}) were determined at different temperatures from the respective calibration plots as the intercepts of these plots at pPD = 0, and used to determine the isothermal temperature coefficient $(dE^0/dt)_{cell}$ of the cell with the aid of the following equation [37]:

$$E^0_{cell} = E^0_{cell(25\,^\circ C)} + \left(\frac{dE^0}{dt}\right)_{cell}(t - 25)$$

Plot of E^0_{cell} versus $(t - 25)$ produced a straight line. The slope of this line was taken as the isothermal temperature coefficient of the cell. It amounts to 5.2×10^{-4} V/°C.

Plot of $E^0_{electrode}$ versus $(t - 25)$ gave a straight line, its slope was taken as the isothermal temperature coefficient of the electrode $(dE^0/dt)_{electrode}$. It amounts to 3.4×10^{-4} V/°C. The small values of $(dE^0/dt)_{cell}$ and $(dE^0/dt)_{electrode}$ reveal the high thermal stability of the electrode within the investigated temperature range.

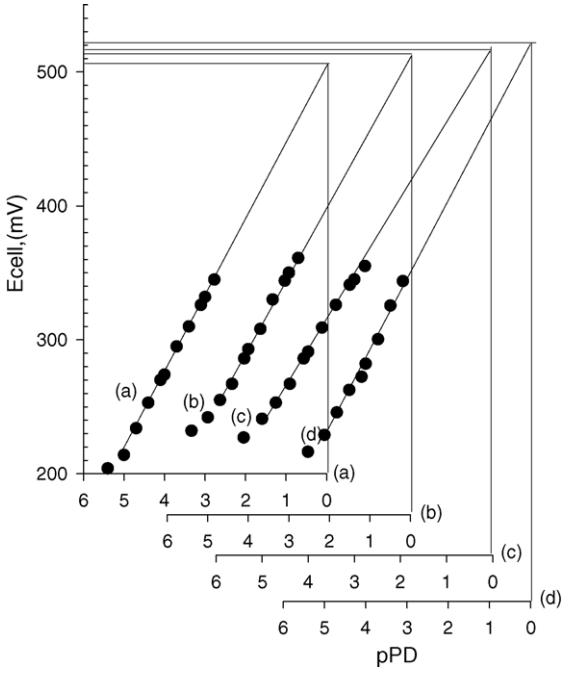

Fig. 4. Calibration graphs for PD-CMCPE at test solution temperature 25 (a), 35 (b), 45 (c) and 55 °C (d).

3.5. Effect of ionic strength on the response of the electrode

The effect of ionic strength (0.1–1.0 M KNO_3) on the calibration graph of PD-CMCPE was investigated. The electrode response is nearly the same within the 0.1–1.0 M KNO_3 solutions. This is indicated by the constant Nernstian behavior and the same linearity range obtained at different ionic strength values. Consequently, no ionic strength value was recommended for measurements with this electrode in batch conditions.

3.6. Electrode response in FIA

In flow-injection measurements using plastic membrane electrodes, in principle a higher level of detection limits is observed relative to batch mode which is due to the difference in dispersion coefficients between the two modes and the too short time of contact between the sample and the electrode in case of FIA [38]. Generally, it well known that the higher limits of detection of conventional plastic membrane electrodes compared to CMCPEs are mainly due to some leakage of internal solutions into the test solutions via the polymeric membranes [39]. Meanwhile, the very low Ohmic resistance of CPEs and hence the higher electrical conductivity than the internal solutions in conventional electrodes is expected to result in lower response time of the CMCPE. With the present PD-CMCPE, in FI system using dispersion coefficient of 1.3, it was possible to detect as low as 7.3×10^{-7} M PD with response time not more than 5 s. It seems that the lower response time in FIA mode compared to batch mode enhances electrode sensitivity in FIA by nullifying the negative effect of the short contact time.

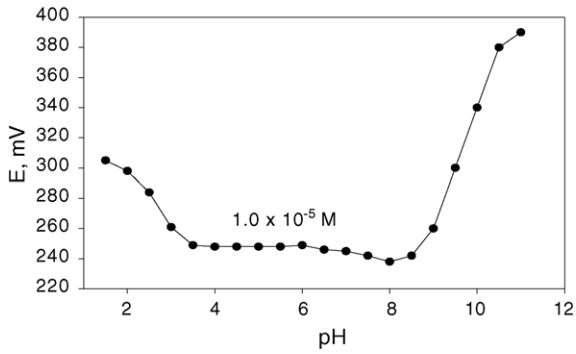

Fig. 5. Effect of pH of the test solution on the potential response of PD-CMCPE.

3.7. Effect of pH

The effect of pH of the test solution on the electrode potential was studied in batch and FIA measurements. In batch measurements, the variation in potential with pH change was followed by the addition of small volumes of (0.1–1 M) of HCl and NaOH to a series of PD solutions of different concentrations. As can be seen from the results shown in Fig. 5, the potential variation due to pH change is considered acceptable in the pH range 3.5–6.0. Nevertheless, at pH values lower than 3.5, the potential slightly increases, which can be related to interference of hydronium ions, while the increase that takes place at pH values higher than 8.0 is most probably attributed to the interference caused by Na^+ ions.

In FIA, a series of solutions of concentration that is 10^{-2} M PD and pH ranging from 1 to 8 is injected in the flow stream, and then the peak heights, representing the variation of potential response with pH, were measured. No remarkable variation in the peak heights was observed in the pH range 3.5–6.0.

3.8. Selectivity of the electrode

The influence of some inorganic cations, organic cations, sugars, and amino acids on the PD-CMCPE was investigated. In the batch conditions, the matched potential method was applied [40,41]. Among the different mixed solution methods, the matched potential method is unique in that it depends neither on the Nicolsky-Eisenman equation nor on any of its modifications. This method was recommended in 1995 by IUPAC as a method that gives analytically relevant practical selectivity coefficient values. To determine the selectivity coefficient of different interfering ions for PD-CMCPE, the potential of a reference solution of PD was measured and specified amounts of PD (a_{PD}) in the range of 2×10^{-4} to 5×10^{-5} M were added to the reference solution, the potential was measured and the corresponding potential change (ΔE) is recorded. In a separate experiment, the interfering

Table 3
Selectivity coefficient $-\log K^{\text{Pot}}_{\text{PD,J}^{Z+}}$ for PD-CMCPE

Interferent	Steady state	FIA	Interferent	Steady state	FIA
Na^+	3.15	4.03	Cr^{3+}	2.54	2.84
NH_4^+	3.23	3.92	Thiamine HCl	2.64	3.12
K^+	3.05	3.88	Pyridoxine HCl	3.21	3.56
Mg^{2+}	2.89	3.56	Glucose	4.12	–
Mn^{2+}	3.22	4.33	Maltose	3.59	–
Cd^{2+}	3.46	4.30	Fructose	3.81	–
Ba^{2+}	3.25	4.52	Lactose	3.95	–
Ca^{2+}	2.95	3.77	Glycine	2.65	–
Sr^{2+}	2.42	3.41	Asparagine	3.21	–
Zn^{2+}	2.91	3.78	DL-serine	2.56	–
Cu^{2+}	3.24	3.33	DL-leucine	2.68	–
Ni^{2+}	3.09	4.42	Maltose	3.59	–

ions (J) (in the range of 1.0×10^{-1} to 1.0×10^{-2} M) were successively added to an identical reference solution of PD until the change in potential matched the ΔE value. The values of $K^{\text{Pot}}_{\text{PD,J}^{Z+}}$, are then calculated using the following equation:

$$K^{\text{Pot}}_{\text{PD,J}^{Z+}} = \frac{a_{\text{PD}}}{a_{\text{J}}}$$

where a_J is the activity of the added interferent.

In FI conditions, the values of selectivity coefficients were calculated based on potential values measured at the tops of the peaks for the same concentrations of the drug and the interferent according to the separate solution method [42], since the matched potential and other mixed solution methods, in this case are time consuming due to the needs of many solutions and perform many steps. The selectivity coefficient values of the electrode listed in Table 3 reflect a very high selectivity of this electrode for piribedil cation.

The mechanism of selectivity is mainly based on the stereospecificity and electrostatic environment and it is dependent on how much fitting is present between the locations of the lipophilicity sites in the two competing species in the bathing solution side and those present in the receptor of the ion-exchanger [43]. Inorganic cations do not interfere because of differences in ionic size, mobility and permeability. The electrode is also selective to PD^+ over a number of sugars, amino acids, and organic cations namely thiamine and pyridoxine hydrochlorides.

3.9. Analytical applications

In order to evaluate the applicability of the proposed PD-CMCPE, piribedil in its pharmaceutical preparation (Trivastal®) and in urine samples spiked with known amounts of PD was determined using this electrode in batch an FI conditions.

In batch mode, the PD content of these samples was determined applying the standard additions method to overcome the matrix effects. With FI system, the samples were analyzed by measuring the peak heights, and then compared to those obtained from injecting standard solutions of pure PD. The results of applying the above methods are compared with the values obtained from the reference spectrophotometric method [22]. *F*-test was used for comparing the precisions of the two methods and *t*-test for comparing accuracy [44]. The calculated *F*- and *t*-values (Table 4) were less than the critical (tabulated) ones. Thus, there is no significant difference between the precisions or the accuracies of the two methods at 95% confidence levels.

Table 4
Recovery of PD from Trivastal (tablets) and urine samples using PD-CMCPE

Sample	M	% Recovery	R.S.D.%	$F^{3,3}$ value (9.28)	*t*-values
Tablets batch	6.63×10^{-5}	99.1	0.31	4.65	2.34
	2.57×10^{-4}	99.6	1.21	6.83	1.25
	3.79×10^{-4}	98.9	0.53	2.70	3.24
FIA	5.00×10^{-5}	101.0	1.03	1.10	2.78
	5.00×10^{-4}	98.8	0.72	3.86	1.89
Urine batch	6.00×10^{-5}	100.7	0.98	–	–
	4.00×10^{-4}	98.3	1.45	–	–
	1.00×10^{-3}	101.0	1.32	–	–
FIA	5.00×10^{-5}	100.8	0.75	–	–
	5.00×10^{-4}	100.0	1.12	–	–

M: the molar concentration of PD samples (taken). R.S.D.: relative standard deviation.

Table 5
Linear regression analysis for potentiometric determination of PD in batch and FIA conditions

Sample	Intercept of regression line[a]	Slope of regression line	Correlation coefficient (r)
Tablets (20 mg/l)	0.051[b]	0.998	0.999
	0.093[c]	0.982	
Urine	−0.099[b]	0.998	0.999
	0.097[c]	0.992	

[a] Recovered vs. taken.
[b] Standard additions method.
[c] FIA conditions.

The results obtained from the potentiometric determination of the drug in batch and FI conditions were subjected to linear regression analysis (Table 5), in order to establish whether the investigated electrode exhibits any fixed or proportional bias. On plotting the amounts of PD taken versus the amount recovered a regression line was obtained in each case with a slope of 0.990 ± 0.008, an intercept of near zero ($0.075 \pm 0.024\%$) and a correlation coefficient near unity (0.999). These values revealing the absence of any systematic error during the measurements within the investigated concentration range.

4. Conclusions

The proposed chemically modified carbon paste electrode based on piribedil phosphomolybdate as the electroactive compound might be a useful analytical tool and an interesting alternative for the determination of (PD^+) in different real samples. The present electrode shows high sensitivity, reasonable selectivity, fast static response, long-term stability and applicability over a wide pH range with minimal sample pretreatment. The PD-CMCPE showed wider linear range and lower limits of detection relative to the previously described electrodes of the conventional type [24,25]. The reported methods of determination with the prescribed electrode are simple, sensitive, highly specific and advantageous over many other procedures for PD determinations, since the interference of the recipients, impurities, degradation product or other accompanying drugs is nullified.

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