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Carbon Paste Electrode for the Potentiometric Flow Injection Analysis of Drotaverine Hydrochloride in Serum and Urine

Yousry M. Issa, Hosny Ibrahim*, and **Hazem M. Abu-Shawish**

Chemistry Department, Faculty of Science, Cairo University, Cairo, Egypt

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Abstract. A carbon paste electrode for drotaverine hydrochloride (DvCl) was prepared and fully characterized in terms of composition, life span, usable pH range, response time and temperature. The electrode was applied to the potentiometric determination of drotaverinium ions in pharmaceutical preparations and biological fluids in steady state and flow injection conditions (FIA). The electrode is based on a mixture of two ion exchangers, namely, drotaverinium-silicotungestate and drotaverinium-tetraphenylborate dissolved in tricresyl phosphate as pasting liquid. The modified electrode showed a near-Nernstian slope of 59.34 ± 2 mV over the concentration range of 5.0×10^{-7}–1.0×10^{-2} M. The electrode exhibits good selectivity for DvCl with respect to a large number of inorganic cations, organic cations, sugars and amino acids. Potentiometric titrations of DvCl with several titrants have been monitored using this modified carbon paste electrode as an end-point indicator electrode. The proposed electrode offers the advantages of simplicity, accuracy, automation feasibility and applicability to turbid and colored samples.

Key words: Drotaverine hydrochloride; carbon paste electrode; FIA; biological fluids; potentiometric determination.

Chemically modified carbon paste electrodes (CMCPEs) have been successfully applied as potentiometric sensors for the 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 a 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 [6–8] and voltammetry [9–11], in addition to potentiometry [12, 13].

Drotaverine [1-(3,4-diethoxybenzylidene)-6,7-diethoxy-1,2,3,4-tetrahydroiso-quinoline] [985-12-6], a hydrated derivative of papaverine, is an effective spasmolytic agent [14]. This drug is capable of relieving spasms of various organs, regardless of their function and innervation. Drotaverine has been proved to be superior in its efficiency to papaverine and it is also more reliably absorbed after oral administration [15, 16]. It is used in the symptomatic treatment of various conditions, e.g. gastrointestinal diseases, biliary dyskinesia, nephrolithiasis, gynaecological diseases and vasomotor diseases associated with smooth muscle spasms [17, 18]. It can also be used as an adjuvant to hypotensive agents in acute disturbances of blood

* Author for correspondence. E-mail: dr_hosny@yahoo.com

pressure in hypertensive disease, angina pectoris and coronary spasms [19].

The reported methods for the determination of drotaverine are mainly chromatographic, and although they are highly sensitive, they are also very expensive, involve the use of complex procedures with several sample manipulations, and require long analysis times. Besides, none of them are easy to automate. They include high-performance liquid chromatography [20–23] and thin layer chromatography [2]. Other alternatives include spectrophotometry [24], differential spectrophotometry [25, 26], computer-aided spectrophotometry [27] and square-wave polarography [28]. The spectrophotometric methods of drug analysis usually suffer from poor selectivity.

In spite of progress in the design of highly selective electrodes for various ions, there has not been any report on the development of selective and sensitive drotaverine sensors. This paper describes the construction, potentiometric characterization, and analytical application of a drotaverine-chemically modified carbon paste electrode (Dv-CMCPE) based on the use of a mixture of two ion-exchangers, drotaverinium-silicotungestate and drotaverinium-tetraphenylborate as electroactive materials and tricresyl phosphate (TCP) as plasticizer.

Experimental

Reagents and Solutions

Drotaverine hydrochloride was obtained from Alexandria Co. for Pharmaceutical and Chemical Industries (Alexandria, Egypt). The stock solution was prepared to contain 0.01 mol L^{-1} DvCl and standardized by differential ultraviolet spectrophotometry [26]. The pharmaceutical preparations containing DvCl (Do-Spa, tablets and ampoules) were obtained from local drug stores. Graphite powder, dibutyl phthalate (DBP), dioctyl phthalate (DOP), dioctyl sebacate (DOS), tricresyl phosphate (TCP) and diisononyl phthalate (DINP) were used as received from Aldrich. For the preparation of ion exchangers and potentiometric titrations, aqueous solutions of silicotungstic acid (STA), silicomolybdic acid (SMA), phosphotungstic acid (PTA), phosphomolybdic acid (PMA) and sodium tetraphenylborate (NaTPB) (all in concentrations of 0.01 M) were prepared from materials of analytical grade purity. The exact concentrations of these solutions were determined by the appropriate methods recommended [29–31]. When the samples were analyzed using FIA, they were initially diluted with water, as pH and ionic strength adjustment were achieved within the flow system.

Preparation of Ion-Exchangers

The ion-exchangers drotaverinium silicotungstate (Dv-ST) and drotaverinium tetraphenylborate (Dv-TPB) were prepared by adding 100 mL of 10^{-2} M DvCl hot solution to the appropriate volume of 10^{-2} M solution of STA and NaTPB. The formed precipitates were filtered off, washed thoroughly with distilled water, dried at room temperature and ground to fine powders. The exact chemical compositions of these precipitates were elucidated by elemental and spectral methods of analysis.

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 Dv-ST, Dv-TPB and 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 a weighed amount of tricresyl phosphate. 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.

Apparatus

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 packed saturated calomel electrode (SCE) was used as an external reference electrode. The electrochemical system is represented as follows:

Dv-CMCPE/test solution/SCE

A single-stream FIA 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 an 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 Zonen (Delft, Netherlands).

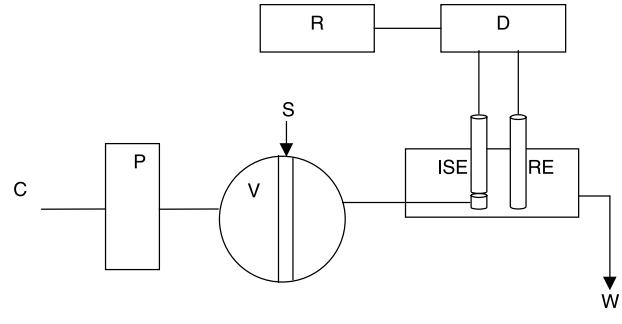

Fig. 1. Single-stream FIA manifold for DvCl determination; *C* carrier solution; *S* sample; *P* peristaltic pump; *V* injection valve; *ISE* Dv-electrode; *RE* reference electrode; *D* detector; *R* recorder; *W* waste

Potentiometric Determination of DvCl

The standard addition method [32] was applied: small increments (50–100 µL) of standard DvCl solution (10^{-1} M) were added to 50 mL aliquot samples of various concentrations from the drug sample solution equivalent to 0.399–43.4 mg DvCl. The change in potential at (25 ± 0.1 °C) was recorded for each increment, and this data was used to calculate the concentration of DvCl in the sample solution.

Determination of DvCl in Do-Spa Tablets

The contents of 15 tablets (40 mg DvCl/tablet) of Do-Spa were powdered, and an accurately weighed portion equivalent to 200 mg was mixed with 50 mL doubly distilled water, shaken in a mechanical shaker (Burrell Corp.) for about 24 h and then filtered into a 100 mL measuring flask. The solution was completed to the mark with doubly distilled water, and the container was shaken. Different volumes of the solution (1.0–10.0 mL) were taken and subjected to the standard addition method.

Determination of DvCl in Biological Fluids

Different quantities of DvCl and 1 mL serum or 5 mL urine were transferred to a 50 mL measuring flask and completed to the mark with 1×10^{-4} M HCl to give solutions of pH values ranging from ~4–5 and concentrations of 6.0×10^{-7} to 2.8×10^{-5} M DvCl. These solutions were subjected to the standard addition method for the potentiometric determination of DvCl.

Potentiometric Titration

An aliquot of DvCl solution containing 2.17–65.12 mg DvCl was transferred into a 100 mL beaker, diluted to approximately 50 mL with distilled water and then titrated against a standard solution of STA, SMA, PTA, NaTPB or NaOH. The end points were determined from the S-shaped curve by first and second derivative plots.

Results and Discussion

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 towards the Dv^+ ion, whereas, in the presence of the proposed ion exchangers, the optimized sensors demonstrated an appreciable response and remarkable selectivity for Dv^+ over several common inorganic and organic cations. The best results were obtained when the paste was modified by a mixture of two ion exchangers, namely, Dv-ST and Dv-TPB with a weight-to-weight (w/w) ratio of 3:7. The potentiometric response of the electrodes modified by either Dv-ST or Dv-TPB alone was found to be non-satisfactory, while in the presence of a mixture of both the response was greatly improved. The presence of such a mixture not only improves the response behavior and selectivity but also enhances the sensitivity of the electrode.

Apart from the critical role of the nature and the amounts of ion exchangers used in preparing CMCPEs, some other important features, such as the nature of the solvent mediator, the plasticizer/graphite ratio and the nature of any additives used, are known to significantly influence the sensitivity and selectivity of the prepared electrode [33–35].

The influence of the plasticizer type and concentration on the characteristics of the Dv-sensor was investigated by using five plasticizers with different polarities including DBP, DOP, DOS, TCP and DINP. Different plasticizer/graphite (w/w) ratios were studied; the 1:1 plasticizer/graphite ratio produced maximum sensitivity for all of the plasticizers. As is quite obvious from emf-pDv 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^{-1}, 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 Dv^+ ion

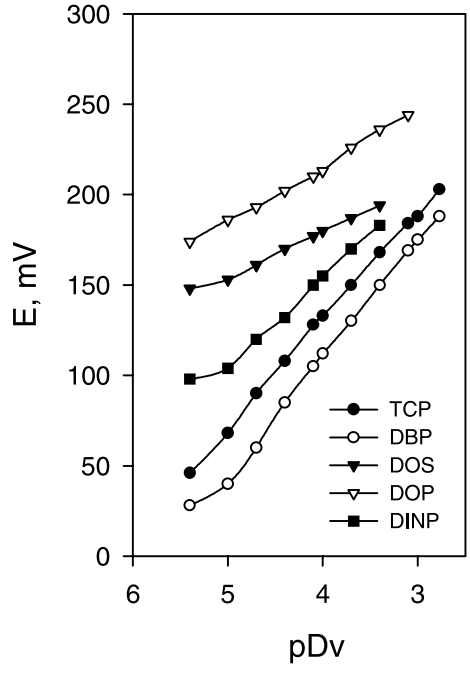

Fig. 2. Effect of different plasticizers on the potential response of Dv-CMCPE

Table 1. Response characteristics of the Dv-CMCPE electrode

Parameter	Steady state	FIA
Electrode composition	Mixed ion-exchangers (7.0% Dv-ST + 3.0% Dv-TPB), 46.0% graphite and 44.0% TCP	
Slope (mV decade^{-1})	59.34 ± 2	61.9 ± 2
Correlation coefficient	0.998	0.980
Lower detection limit (M)	5.0×10^{-7}	5.0×10^{-7}
Working pH range	2.5–7.0	2.5–7.0
Response time (sec.)	$\leq$3–7	$\leq$6–10

into the paste prior to its exchange with the soft ion exchanger. An electrode modified by 7% Dv-ST, 3% Dv-TPB (w/w) with 44% TCP as plasticizer has a slope of 59.3 ± 2 mV concentration decade^{-1} and a wide range of linearity, 5.0×10^{-7}–1.0×10^{-2} M. This electrode was selected, and its electrochemical performance characteristics in both steady state and FIA conditions were systematically evaluated according to IUPAC recommendations [36]. The results are summarized in Table 1.

The dynamic response time [36] 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 DvCl solutions, each having a 10-fold increase in concentration from 1.0×10^{-5} to 1.0×10^{-2} M. The electrode yielded steady potentials within 3–7 s. The potential reading stays constant (± 1 mV) for at least 15 minutes. A typical potential-time plot for the response of the electrode is shown in Fig. 3.

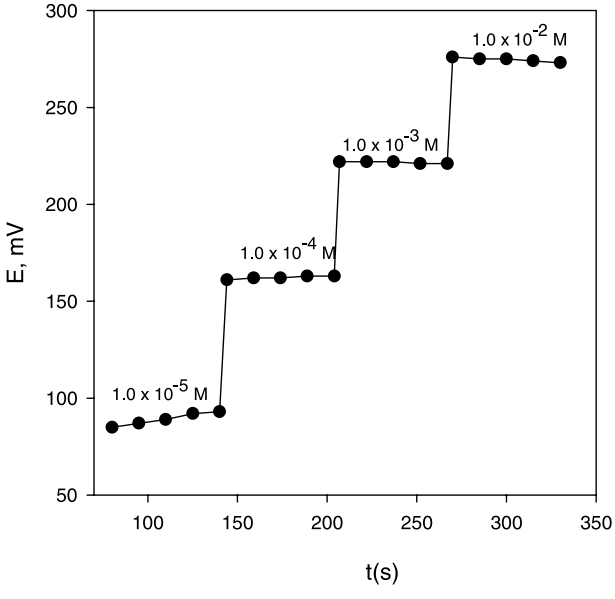

Fig. 3. Typical potential-time plot for the response of the Dv-CMCPE

The repeatability of the potential reading of the electrode was examined by subsequent measurements in 1×10^{-3} M DvCl solution immediately after measuring the first set of solutions at 1.0×10^{-4} M DvCl. The standard deviation for 5 replicate measurements of emf was found to be 1.142 in 1.0×10^{-4} M solution and 0.707 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 section from the master paste was found to function perfectly.

Effect of Temperature

To study the thermal stability of the electrode, calibration graphs (electrode potential, E_{elec} vs pDv) were constructed at different test solution temperatures covering the range of 25–55 °C. The isothermal coefficient (dE_{elect}/dt) of the electrode was calculated [37] and found to be 0.0001 V °C^{-1} and (dE_{cell}/dt) equals 0.0006 V °C^{-1}. These values indicate a fairly high thermal stability of the electrode within the temperature range investigated and show no deviation from the theoretical Nernstian behavior.

Optimization of FIA Response

The working characteristics of the Dv-CMCPE were assessed using a low dispersion FIA manifold (Fig. 1). The carrier stream was 0.033 M Na_2SO_4 solution. In order to stabilize the base line, a fixed DvCl concentration (1×10^{-7} M) was used.

The effects of sample size and flow rate on Dv-CMCPE were examined by injecting different volumes (9.4–500 µL) of 1×10^{-3} M DvCl solutions at different flow rates. The sample loop of size 75 µL with a flow rate of 5.35 mL min^{-1} were found to be the optimum and were thus used throughout this work. Figure 4 shows a representative plot for the recording and the calibration graph obtained for Dv-CMCPE in optimum FIA conditions.

Effect of pH

The effect of the pH of the test solution on the electrode potentials was studied in steady state and FIA measurements. In steady state measurements, the variation in potential with pH change was followed by the addition of small volumes (0.1–1 M) of HCl and

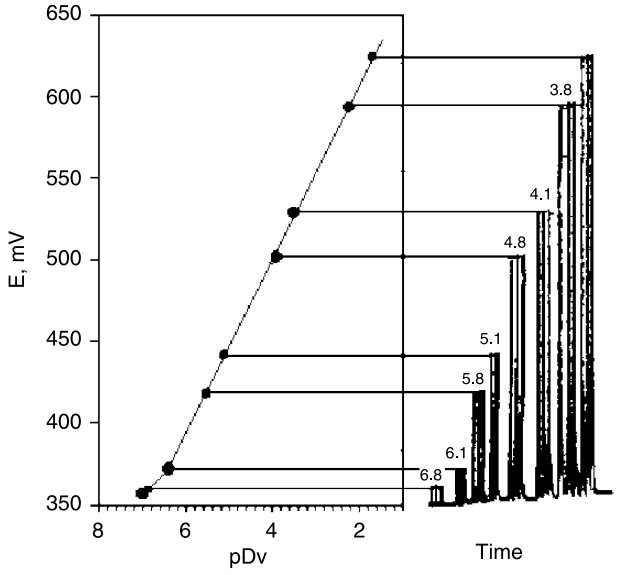

Fig. 4. Recordings and calibration graph of DvCl under optimum FIA conditions

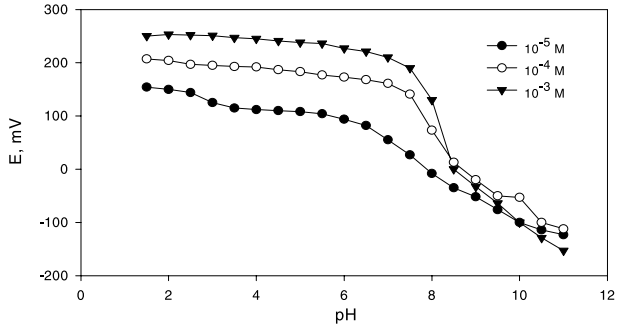

Fig. 5. Effect of pH on the response of Dv-CMCPE in steady state measurements

NaOH to a series of DvCl 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 of 2.5–7.0. Nevertheless, at pH values lower than 2.5, the potential increases slightly, which can be related to interference of hydronium ions, while the decrease that takes place at pH values higher than 7.0 is most probably due to the formation of the free drotaverine base in the test solution.

In FIA measurements, a series of solutions with a concentration of 10^{-3} M DvCl was injected into flow streams of different pH values ranging from 1–8, whereupon the peak heights, representing the variation of potential response with pH, were measured. No remarkable variation in the peak heights were observed in the pH range of 2.5–7.0.

Selectivity of the Electrode

The influence of some inorganic cations, organic cations, sugars, urea and amino acids on the Dv-CMCPE was investigated. In the steady state conditions, the matched potential method was applied [38, 39]. 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, specified amounts of DvCl (a_{Dv}) in the range of 2×10^{-4}–5×10^{-5} M were added to a reference solution of DvCl, and the corresponding potential change (ΔE) was measured. In a separate experiment, the interfering ion (J) (in the range of 1×10^{-1}–1.0×10^{-2} M) was successively added to an identical reference solution until the change in potential matched the ΔE value. The values of $K^{pot}_{Dv,J^{z+}}$ were then calculated using the following equation:

$$K^{pot}_{Dv,J^{z+}} = (a_{Dv}/a_J)$$

In FI conditions, the values of the 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 [40]. The matched potential and other mixed solution methods would in this case be time-consuming since many solutions would be required and many steps would need to be performed. The selectivity coefficient values of the electrodes $-\log K^{pot}_{Dv,J^{z+}}$ listed in Table 2 reflect a very high selectivity of these electrodes for the drotaverinium cation. The mechanism of selectivity is mainly based on the stereospecificity and electrostatic environment, and it is dependent on how much fitting there is between the locations of the lipophilicity sites in the two competing species on the bathing solution side and those present in the receptor of the ion exchanger [41]. Inorganic cations do not interfere because of differences in ionic size, mobility and permeability. The electrode is also selective to Dv^+ over a number of sugars, amino acids, and organic cations, namely thiamine and pyridoxine hydrochlorides. The electrode suffers from interference by papaverinium ion. This may be attributed to the close similarity between the chemical structures of both papaverine and drotaverine, and thus similar interaction of these lipophilic

Table 2. Selectivity coefficients $-\log K^{pot}_{Dv,J^{z+}}$ values for Dv-CMCPE

Interferent	Steady state	FIA	Interferent	Steady state	FIA
Na^+	3.61	2.40	Glucose	4.00	2.47
NH_4^+	3.85	2.75	Maltose	3.95	2.70
K^+	3.55	2.20	Fructose	3.98	2.80
Mg^{2+}	3.65	2.80	Lactose	1.58	2.01
Mn^{2+}	3.70	2.19	Glycine	3.17	2.50
Cd^{2+}	3.80	2.79	Asparagine	3.90	3.67
Ba^{2+}	3.57	2.75	DL-serine	3.77	3.35
Ca^{2+}	3.44	2.45	DL-leucine	2.80	2.41
Sr^{2+}	3.33	2.85	Pyridoxamine HCl	1.22	1.25
Zn^{2+}	2.60	2.55	Papaverine HCl	0.564	–
Cu^{2+}	2.80	2.70	Vit. C	1.52	–
Ni^{2+}	3.60	2.30	Urea	1.22	–
Al^{3+}	2.70	2.50			
Cr^{3+}	2.50	2.40			

cations with the ion exchanger. Fortunately, papaverine is not present in the formulations of drotaverine. For this reason, they do not prejudice the quality of the determinations.

Comparing the selectivity coefficient values obtained for the investigated electrodes in both steady state and FI conditions (Table 2), it is obvious that there is an appreciable difference between the values obtained for each interfering ion in both cases. It was shown earlier for solid state membrane electrodes that apparent selectivity coefficients measured in transient flow injection conditions may differ significantly from those measured in steady state conditions [42, 43]. This is interpreted in terms of difference in time of interaction of interferents with the paste in comparison to the main sensed ion; also the interference process is highly dependent on the rate of diffusion and the exchange reaction of the interfering ion [44]. Therefore, in FI measurements, where the sample remains in contact with the electrode for a short period of time, the apparent selectivity usually differs from that found in steady state conditions.

Analytical Applications

The investigated Dv-CMCPE was found to be useful in the potentiometric determination of DvCl in tablets and ampoules (Do-Spa) by direct potentiometry or potentiometric titration. In contrast to direct potentiometry, the potentiometric titration technique usually offers the advantage of high accuracy and precision, albeit at the cost of increased titrant consumption. A further advantage is that the potential break at the titration end-point must be well defined, but the slope of the sensing electrode response neither needs to be reproducible nor Nernstian, and the actual potential value at the end points is of secondary interest. The method for drotaverinium ion (Dv^+) titration is based on the decrease of (Dv^+) concentration by precipitation with STA, SMA, PTA, NaTPB or NaOH standard solution. The titration process was carried out manually in aqueous solutions containing 2.17–65.1 mg DvCl with average recoveries of 97.83–101.5% and relative standard deviations of 0.84–1.84% for 5

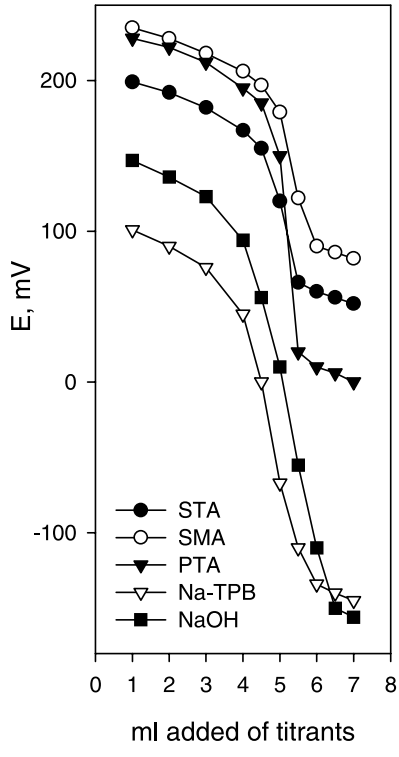

Fig. 6. Curves of the potentiometric titration of 21.7 mg DvCl with different titrants using Dv-CMCPE

measurements. The sudden emf peaks near the end points amount to approximately 135 mV when titrating 2.17 mg DvCl, and it increases gradually as the titrated amounts of DvCl increase, reaching 260 mV on titrating 21.7 mg DvCl. This reflects a very high degree of completeness of the titration reactions. Corresponding titration curves show well-developed sudden titration peaks (Fig. 6).

There are only very few reports in the literature describing the measurement of drotaverine in plasma. ^{14}C-Labeled drotaverine was used to study the pharmacokinetics of the drug in mice [45] and humans [46]. Clinical pharmacological studies indicated that the drug is absorbed rapidly and the principle routes of elimination are the urine (40% of the dose) and feces (47%) [47]. A comparative bioavailability study [48] where an oral dose of 40 mg DvCl was given to healthy volunteers indicated that the mean maximum concentration of the drug in plasma is $\sim 197.6 \pm 58.8\ \text{ng mL}^{-1}$. The levels of DvCl in plasma in this bioavailability study were determined by extraction HPLC [22]. A simple method is required to determine drotaverine in serum and urine following its administration at normal therapeutic dose levels to human subjects in order to carry out bioavailability studies on different dose forms of drotaverine. With the present method, DvCl was determined in serum and urine samples spiked with known amounts of the drug to give concentration ranges matching the normal, clinically relevant levels. The standard addition technique was applied to overcome the matrix effects in these real samples.

With the FI system, different samples were analyzed, including biological fluids spiked with known amounts of DvCl, dissolved drug tablets or infusion solutions. The peak heights were measured, and then compared to those obtained when injecting standard amounts from pure DvCl. The results obtained from the potentiometric determination of the drug in these real samples in both steady state and FI conditions are given in Table 3. The results of the recoveries of DvCl applying the standard addition method, potentiometric titration, and FIA were evaluated statistically and compared with the values obtained with the spectrophotometric method [26] by applying the F-tests [49]. The values obtained (Table 4) show that the present methods have a precision comparable to that of the

Table 3. Recovery of DvCl from Do-Spa (tablets), spiked serum and urine samples by proposed Dv-CMCPE

Sample	Steady state			FIA		
	DvCl (M)			DvCl (M)		
	Taken	Found	% Recovery	Taken	Found	% Recovery
Tablets (Do-Spa)	9.1×10^{-5}	$(9.20 \pm 0.2) \times 10^{-5}$	101.1	9.1×10^{-5}	$(8.90 \pm 0.1) \times 10^{-5}$	97.8
	9.1×10^{-4}	$(9.30 \pm 0.3) \times 10^{-4}$	102.2	9.1×10^{-4}	$(9.00 \pm 0.2) \times 10^{-4}$	98.9
	1.8×10^{-3}	$(1.80 \pm 0.1) \times 10^{-3}$	100.5			
Serum	6.0×10^{-7}	$(5.50 \pm 0.2) \times 10^{-7}$	91.6	8.0×10^{-7}	$(7.70 \pm 0.1) \times 10^{-7}$	96.3
	8.0×10^{-7}	$(7.60 \pm 0.2) \times 10^{-7}$	95.0	1.0×10^{-6}	$(1.01 \pm 0.1) \times 10^{-6}$	101.0
	1.0×10^{-6}	$(1.02 \pm 0.1) \times 10^{-6}$	102.0			
Urine	5.0×10^{-6}	$(5.10 \pm 0.2) \times 10^{-6}$	102.0	5.0×10^{-6}	$(4.90 \pm 0.2) \times 10^{-6}$	98.0
	1.8×10^{-5}	$(1.81 \pm 0.1) \times 10^{-5}$	100.5	1.8×10^{-5}	$(1.82 \pm 0.1) \times 10^{-5}$	101.1
	4.0×10^{-5}	$(3.90 \pm 0.1) \times 10^{-5}$	97.5	4.0×10^{-5}	$(3.90 \pm 0.1) \times 10^{-5}$	97.5

Table 4. Statistical treatment of data obtained for the determination of DvCl using the Dv-CMCPE

Method	Pure solution			Ampoule		
	X ± S.E.	Relative error (%)	$F^{3,3}$ value (9.28)	X ± S.E.	Relative error (%)	$F^{3,3}$ value (9.28)
Official method	99.22 ± 0.008	0.78		100.9 ± 0.014	0.90	
Method (I)	100.1 ± 0.029	0.100	0.625	99.80 ± 0.035	0.200	0.930
Method (II)	100.6 ± 0.033	0.600	0.900	100.9 ± 0.153	0.900	5.852
Method (III)	98.0 ± 0.049	0.200	1.806	101.8 ± 0.462	1.800	1.225

X ± S.E.: recovery ± standard error.
Method (I): standard addition method, *Method (II)*: potentiometric titration, *Method (III)*: FIA.

spectrophotometric method [26]. However, the proposed methods are more practical regarding time of analysis, consumption of solvents and sample pretreatment requirements for spectrophotometric or chromatographic analysis of DvCl.

Conclusions

The proposed chemically modified carbon paste electrode based on a mixture of two ion exchangers, namely drotaverinium-silicotungestate and drotaverinium-tetraphenylborate as the electroactive compounds, might be a useful analytical tool and an interesting alternative in the determination of (Dv^+) 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 reported methods of determination using the proposed electrode are simple, sensitive, highly specific and advantageous over the previously described procedures for DvCl determinations, since interferences from the recipients, impurities, degradation products or other accompanying drug components are eliminated. Accuracy of analysis with the proposed procedures is significantly greater than with the classical spectrophotometric method.

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