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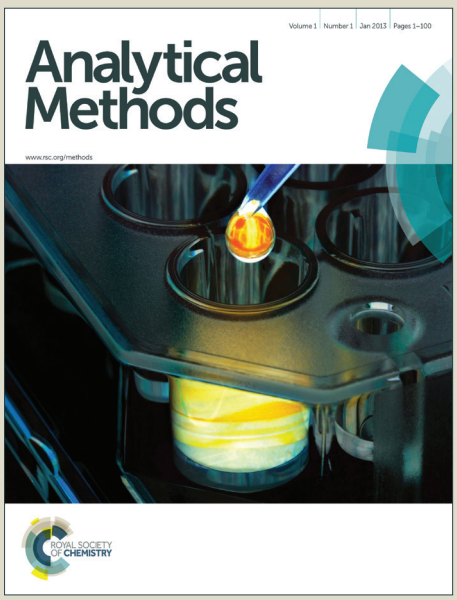

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A new Potentiometric Sensor for Determination of ketamine Hydrochloride in Ampoules and Urine

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Significance, Novelty and Wider Societal Impact of the Work Reported

Ketamine drug is a colorless, odorless, tasteless, hallucinogenic and anesthetic commonly used for animals and human. It is used by youth in recreational parties for sedation and misused in drug-facilitated crimes for its pharmacological properties. Thus, there is critical need for the development of selective, inexpensive diagnostic tool for the determination of this analyte.

Potentiometric methods employing carbon paste electrodes (CPEs) have attracted attention as ion-selective electrodes mainly due to their advantages over membrane electrodes such as chemical inertness, robustness, renewability, stable response, low Ohmic resistance, no need for internal solution and suitability for a variety of sensing and detection applications. Moreover, CPEs belong to nontoxic and environmentally friendly electrodes. In their case, problems with passivation are simply eliminated by a simple and quick renewal of their surface. Due to the above mentioned properties, carbon paste electrode seems to be especially promising.

On careful review of the literature, there is no report on determination of ketamine hydrochloride using a carbon paste electrode.

The present work describes construction, potentiometric characterization, and analytical application of a new modified carbon paste electrode selective for ketamine drug based on ion-exchanger of ketamine hydrochloride with sodium tetraphenylborate as electroactive materials and tris(2-ethylhexyl) phosphate as a plasticizer. The electrode exhibits near Nernstian slope, wide concentration range, low detection limit and short response time. This electrode was used successfully for determination of ketamine ion in ampoules and urine samples.

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Ketamine drug in urine and pharmaceutical preparations was determined by a new chemically modified carbon paste electrode (CMCPE) based on ion-exchanger of ketamine hydrochloride with sodium tetraphenylborate (KT-TPB) as a chemical modifier. The best performance was exhibited by the electrode having the paste containing 0.5 wt% ion-exchanger (KT-TPB), 54.3 wt% graphite, 45.2 wt% tris(2-ethylhexyl) phosphate (TEPh) and 0.2 wt% sodium tetraphenylborate (Na-TPB). The prepared electrode showed a Nernstian slope of 58.9±0.3 mV/decade for ketamine ions in the concentration range 9.0×10^{-6} - 1.0×10^{-2} M with the limit of detection of 7.3×10^{-6} M. The electrode has a short and stable response time 8 s, good reproducibility and it can be used in pH range of 4.0-8.5. The selective coefficients were determined in relation to several inorganic, organic ions, sugars and some common drug excipients. Ketamine is determined successfully in ampoule and urine using the standard additions and the calibration curve methods.

Keywords: Ketamine hydrochloride; ion-selective electrode; potentiometry; carbon paste electrodes; pharmaceutical formulation

Introduction

Ketamine hydrochloride (KTCl), [2-(2-chlorophenyl)-2-(methylamino) cyclohexanone hydrochloride], a general anaesthetic, was first synthesized in 1962 as an alternative to its analogue, phencyclidine [1]. KTCl is an odorless, tasteless and colorless drug and it can be added to beverages, without being perceived by the victim, promoting stupor and sedation together with amnesia. Because of its pharmacological properties, this drug is also misused by offenders in cases of drug-facilitated crimes (DFC) [2, 3]. Therefore, determination of ketamine drug has important practical meanings.

Several analytical techniques have been used to evaluate ketamine in pharmaceutical products including direct UV–visible spectrophotometry method[4], gas chromatography-mass spectrometry [5-7] high performance liquid chromatography with UV detection (HPLC-UV)[8-10], HPLC-CD-UV[11], liquid chromatography high resolution mass spectrometry (LC–HRMS)[12]. In spite of the high sensitivity of these methods, they are very expensive, involve the use of complex procedure with several sample manipulation, and require long analysis time. Besides, none of them are easy to automate. Thus, there is a critical need for the development of selective, inexpensive diagnostic tool for the determination of this analyte. Analytical methods based on potentiometric detection with ion-selective electrodes (ISEs) can be considered good alternatives for they have the longest history and probably the largest number of applications [13]. For example, polymeric membrane-based ion-selective electrodes (ISEs) which have been described for different analytes [13-33]. ISEs were found effective in analysis of pharmaceutical formulations [13,15,20, 24, 30,33] for their attractive properties of simple design, ease of construction, reasonable selectivity, fast response time, applicability to colored and turbid solutions and possible interfacing with automated and computerized systems[33]. Carbon paste electrodes (CPEs) are considered an important type of ion-selective electrodes notable for their ubiquitous properties that entail advantages over membrane electrodes such as chemical inertness, robustness, renewability, stable response, low ohmic resistance, no need for internal solution and suitability for a variety of sensing and detection applications [34-36]. Moreover, CPEs belong to nontoxic and environmentally friendly electrodes. In their case, problems with passivation are simply eliminated by a simple and quick renewal of

their surface. The operational mechanism of the carbon paste electrodes depends on the properties of the modifier materials used to import selectivity towards the target species [37]. Modified carbon electrodes have been widely used as sensitive and selective sensors in various electroanalytical methods [38].

Two reports on potentiometric determination of Ketamine hydrochloride based on polymeric membranes electrodes have been spotted [39, 40]. The present electrode, as a carbon-paste electrode, has advantages over membrane electrodes as indicated above. However, its detection limit is a little smaller but very close to reported electrodes. Overall, it provides a better alternative over the existing electrodes.

A recent review of the literature found no reports on determination of ketamine-hydrochloride using a carbon-paste electrode. In this work, we describe the construction, performance characteristics and analytical application of a novel ketamine ion selective electrode based on ion-exchanger of ketamine hydrochloride with sodium tetraphenylborate as electroactive materials and tris(2-ethylhexyl) phosphate as a plasticizer. The electrode exhibits near Nernstian slope, wide concentration range, low detection limit and short response time. This electrode was used successfully for determination of ketamine ion in samples of ampoules and urine.

Experimental

Reagents

ketamine hydrochloride (KTCl) was provided by General Administration of Pharmacy, Ministry of Health (Gaza-Palestine). Graphite powder, dioctyl phthalate (DOP), dibutyl phthalate (DBP), tris(2-ethylhexyl) phosphate (TEPh) and dioctyl sebacate (DOS) as well as metal salts were purchased from Sigma-Aldrich (CH-9471 Buchs-Germany) and used as received. Silicotungstic acid (STA), silicomolybdic acid (SMA), phosphotungstic acid (PTA), phosphomolybdic acid (PMA) and sodium tetraphenyl borate (Na-TPB) were obtained from Sigma-Aldrich (CH-9471 Buchs-Germany). Glucose, galactose, fructose, sucrose, ceftriaxone sodium, ampicillin sodium, gentamycine sulphate, hydrocortisone sodium, lasix and diclofine sodium were obtained from local drug stores (Gaza-Palestine).

Apparatus

Potentiometric and pH measurements were made with a Pocket pH/mV Meters, pH315i (Wissenschaftlich-Technische Werkstatten GmbH (WTW), Weilheim, Germany). Saturated calomel electrode (SCE) was used as reference electrode for potential measurements and was obtained from Sigma-Aldrich Co. (St Louis, MO, USA). The emf measurements with the CMCPE were carried out with the following cell notations: Hg, Hg_2Cl_2(s), KCl(sat.)||sample solution|CMCPE

Preparation of ion-exchanger complex

The ion-exchangers, Ketaminium silicotungstate (KT_4-ST), Ketaminium silicomolybdate (KT_4-SM), Ketaminium phosphotungstate (KT_3-PT), Ketaminium phosphomolybdate (KT_3-PM) and Ketaminium tetraphenylborate (KT-TPB), were prepared according to a previously reported method [15, 27], by adding a hot solution of 50 mL of 0.01 M KTCl to 12.5 mL of 0.01 M of one of silicotungstic acid (STA) or silicomolybdic acid (SMA), 16.66 mL of 0.01 M of one of phosphomolybdic acid (PMA) or phosphotungstic acid (PTA) and 50 mL of 0.01 M of sodium tetraphenylborate. The precipitates that formed were filtered off, washed thoroughly with distilled water, dried at room temperature and ground to fine powders. The ion-exchanger complex was used as the active substances for preparing the CMCPEs of ketamine hydrochloride.

Preparation of the modified and unmodified electrode

Modified and unmodified carbon paste electrodes were made according to a general procedure, as described elsewhere [30, 36]. High purity graphite, ion-exchanger and different types of plasticizers were intimately hand mixed in a Petri dish to obtain a very fine paste. A portion of the composite mixture was packed firmly into the end of a disposable polypropylene syringe (ca. 3 mm i.d. and 6 cm long) where electrical contact was established with a copper screw wire. To obtain stable electrochemical response, the outer layer of the carbon paste was renewed before each set of measurements by polishing the surface of the electrode. The sensor became ready for use in potentiometric measurements.

Selectivity Coefficient Determination

The separate solution method (SSM) and the matched potential method (MPM) [41] were employed to determine the selectivity coefficients of the potentiometric sensor towards different species. The following equation was employed in SSM.

$$\log K^{pot}_{KT.,J^{z+}} = \frac{E_2 - E_1}{S} + \log [KT] - \log [J^{z+}]^{1/z}$$

where E_1 is the potential for the surfactant ion, E_2 for the interfering ion J, with charge Z and slope S of the calibration graph.

According to the MPM, the activity of (KT) was increased from $\alpha_{KT} = 1.0\times10^{-5}$ M (reference solution) to $\acute{\alpha}_{KT} = 5.0\times10^{-5}$ M and the changes in potential (ΔE) corresponding to this increase were measured. Next, a solution of an interfering ion of concentration a_J in the range 1.0×10^{-1}–1.0×10^{-2} M was added to a new 5.0×10^{-5} M reference solution until the same potential change (ΔE) was attained. The selectivity factor, for each interferent was calculated using the following equation:

$$K^{Pot}_{KT.,J^{z+}} = \frac{\breve{a}_{KT.} - a_{KT.}}{a_J}$$

where the a_J is the activity of the added interferent.

Sample Preparation

Samples of Ketamine hydrochloride ranging from 9.0×10^{-6} to 1.0×10^{-2} M KTCl were determined by the standard addition, potentiometric titration and the calibration curve methods. The required amount of the stock solution was transferred to a 50-mL volumetric flask and diluted to the mark with distilled water to make 0.01 M solutions of KTCl. Different volumes of these solutions equivalent to 1.0×10^{-5} – 1.0×10^{-2} M were analyzed by the above methods using the present electrode. Each analysis was repeated five times. Ampoules containing 10.0 and 20.0 mg mL^{-1} of KTCl and urine analytes were measured as real samples that contain 2.7×10^{-2} and 5.4×10^{-2} M of KTCl, respectively. Dilute solutions that were 1×10^{-4} and 1×10^{-5} M KTCl in each solution were made by transferring the required amounts to 25-mL volumetric flasks and properly diluted. These solutions were subjected to the standard addition method and the calibration curve method.

Sample Analysis

The standard addition method in which small increments (10–100µl) of (0.1 M) KT solution were added to 25-mL aliquot samples of two concentrations (5.0×10^{-5} and 5.0×10^{-4} M) KTCl was applied. The change in potential at (25±0.1°C) was recorded after each increment and these data were used to calculate the concentration of KT ion in the solution samples. The potentiometric titration of different volumes

of 1.0×10^{-3} and 1.0×10^{-2} M KTCl solution: 5–10 mL equivalent to 1.87–37.4 mg, were transferred to a 25-mL beaker, and titrated with a standard solution of Na-TPB using the prepared KT-TPB as indicator electrode. The end points were determined from the S-shaped curve. In the calibration graph method, different amounts of KT were added to 50.0 mL of water comprising a concentration range from 2.0×10^{-5} 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 KT^{+} activity and the resulting graph was used for subsequent determination of the concentration of drug sample.

Results and Discussion

Composition of the electrode

It is well known that the performance characteristics of a given CMCPE based on ion-exchangers depend to a large extent on the nature and amount of the ion-exchanger complex and their lipophilicities [27], the properties of the plasticizer [42], any additives used [43] and the graphite (G)/plasticizer (P) ratio[44]. Thus, the influences of paste composition, nature and amount of plasticizer and amount of additives such as sodium tetraphenylborate, on the potential response of the proposed sensor were tested and the obtained results are given in Table 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 [45]. The ion-exchangers: KT-ST, KT-SM, KT-PT, KT-PM and KT-TPB were prepared and tested as modifiers for the present electrode. The influences of the amount of the different ketamine ion-exchangers in the carbon paste were investigated and the corresponding results are summarized in Table 1. It is noted that the electrode containing zero percentage of ion-exchanger complexes (sensor No. 1) showed a negligible response towards ketamine cations, whereas in the presence of the ion-exchanger complexes the sensor displayed remarkable selectivity for ketamine cations. The electrode # 4 made of 0.5% (w/w) modifier exhibits the best performance. However, further addition of the modifier, (sensors no. 6 to 10), display somewhat smaller slopes and sensitivity, most probably due to some inhomogeneities and possible saturation of the paste [46].

Effect of plasticizers

The plasticizer, in particular, has a dual function: it acts as a liquifying agent, making the membrane material workable, that is enabling homogenous solubilization and modifying the distribution constant of the ion-exchanger used and sustaining these characteristics on continued use. The proportion of plasticizer must be optimized in order to minimize the electrical asymmetry of the membrane in order to keep the sensor as clean as possible and to stop leaching to the aqueous phase [47, 48]. In addition, the plasticizer influences the mobility of the ion-exchanger through extraction of both ions into the organic phase [49]. Therefore, it is necessary to use plasticizers with different physical parameters such as dielectric constant (ε), lipophilicity (logP_{TLC}) and molecular weight (M.wt). In exploration for a suitable plasticizer for constructing this electrode, we used four plasticizers, with the values of dielectric constants (which is a measure of the molecular polarity), lipophilicity and molecular weight respectively listed in parentheses [44], DOS (εr = 3.9, LogP_{TLC} = 10.1, M.wt. = 427), DOP (εr = 5.1, LogP_{TLC} = 7.0, M.wt. = 391), DBP (εr = 6.4, LogP_{TLC} = 4.5, M.wt. = 278) and DOPh (εr = 4.8, LogP_{TLC} = 10.2, M.wt. = 434), The CPE with TEPh as a solvent mediator (plasticizer) produced the best response, as shown in Table 1 and Figure 1. It is likely due to relatively high molecular weight, low dielectric constant and high lipophilicity that maybe avoid exudation and to considerably affect dissolution of ion-associations within the paste. This effect is due to increasing its partition coefficient and providing suitable mechanical property to it compared with low polarity plasticizers[50].

The influence of anionic additive

The presence of lipophilic anion sites in cation-selective electrode reduces ohmic resistance and improves response behavior and selectivity. In addition, it enhances the selectivity of the paste electrode in case where the extraction capability of the ion-exchanger is poor. Moreover, the lipophilic additive may catalyze the exchange kinetics at the sample-electrode interface [48, 51]. Comparison of the data (electrode # 4 and 5) revealed that the sensitivity of the sensor increased and the slope of the calibration curve increased from 52.3±0.7 to 58.9±0.3 mV/decade with the addition of a trace of Na-TPB (about 0.20 wt%).

Effect of graphite/plasticizer (g/p) Ratio

Different graphite/plasticizer ratios of 0.75, 0.90,1.05, 1.20 and 1.35 using TEPh as plasticizer were tested while keeping the amount of ion-exchanger complex constant (i.e.0.5%) as shown in Table 1. The paste with (G/P) ratio of 1.20 showed

the optimum physical properties and ensured high enough mobilities of their constituents [51] and was found to give the best reproducibility and sensitivity of 58.9 mV per decade over the widest linear concentration range of 9.0×10^{-6} - 1.0×10^{-2} M in comparison to the other ratios tested. Pastes with G/P more than 1.35 produced "crumbly" pastes and those with ratio smaller than 0.75 had a consistency resembling that of "peanut butter", i.e., not workable.

out of the electrodes tested, the electrode containing 45.0% TEPh, 54.3% graphite , 0.5% ion-exchanger (KT-TPB), and 0.20 % of sodium tetraphenylborate (Na-TPB) as additive exhibited the best response characteristics and the lowest detection limit. Therefore, this composition was used to study various operation parameters of the electrode. The electrochemical performance characteristics of these electrodes were systematically evaluated according to the International Union of Pure and Applied Chemistry (IUPAC) recommendations [52]. The performance of the electrode was investigated by measuring the emfs of KTCl solutions with a concentration range of 10^{-7}–10^{-1} M by serial dilution. Each solution was stirred and the potential reading was recorded when it became stable, and plotted as a logarithmic function of KT cation activities as shown in Figure 2.

Effect of pH

The most important factor in the functioning of most ion-selective electrodes is the medium acidity expressed as pH value. The effect of pH on the electrode potential at 25°C of the KTCl solutions was studied in (1.0×10^{-3} M and 1.0×10^{-4} M) over the pH range of 2.0–9.0. 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 2, the potential response remains almost constant over the pH range 3.4–6.5 which can be taken as the working pH range of the electrode. However, there is a slight deviation at pH values lower than 3.4 which may be due to H^+ interference. On the other hand, the potential decreases gradually at pH values higher than 6.5. The decrease may be attributed to hydroxide ions that react with ketamine leading to formation of free drug in the test solution, neutral species, which could not be extracted into the membrane.

Response time, electrode renewal and repeatability 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 [52]. In this work, the response time of the electrode was measured by varying the ketamine concentration over the range 1.0×10^{-5} to 1.0×10^{-2} M. The electrode reaches equilibrium in about ~ 8 s. As shown in Figure 3. To check the effectiveness of surface-renewal, the calibration curve was constructed on a certain surface. The slope was found to decrease slightly from 58.9±0.3 to 56.8±0.7 mV/decade after five times of use. This decrease may be attributed to surface contamination and memory effect. Therefore, the electrode surface should be polished to expose a fresh layer for use. The sensor repeatability was evaluated on the same surface by three successive measurements and resulted in a standard deviation of 0.814 and 1.654 for 1.0×10^{-3} and 1.0×10^{-4} M of ketamine respectively. This indicates that the repeatability of the proposed electrode is satisfactory.

Thermal stability of KT-CPE

The response at different temperatures is an important factor in the characterization of a new sensor [53]. By studying the temperature effect on the sensor it is possible to determine the temperature range in which the sensor can be used. The thermal stability of the senor and the calibration graphs (electrode potential, vs. -log [KTCl, M]) were constructed at different test solution temperatures covering the range 25-55 ºC. The characteristics of the electrode, namely, the slope, LOD and usable concentration range at different test solution temperature, were measured. The results indicate that no appreciable change in the calibration characteristics of the electrodes was observed in the temperature range 25–55C, as shown in Figure 4.

Effect of diverse ions

The selectivity coefficient is a summary of information concerning interferences on the electrode response in analytical applications. The response for the analyte must be as high as possible as compared to the response for foreign substances which must be very small so that the electrode exhibits Nernstian dependence on the concentration of the primary ion over a wide range. The selectivity of the ion-exchanger of the electrode depends on the selectivity of the ion-exchange process at the sensor-test solution interface and the mobilities of the respective ions in the matrix of the sensor. Therefore, the response of the electrode towards different substances and ionic species such as inorganic and organic cations should be measured. In addition, drug formulations may contain flavouring agents,

diluents and excipients, such as maltose, glucose and lactose. The results listed in Table 2 reveal that there were no significant interferences from any of the tested substances due to the differences in their mobilities and permeabilities as compared with KT(I) [54]

Applications

Titration of KTCl solution with Na-TPB

The KT-CMCPE was successfully used as an indicator electrode in the potentiometric titration of 10.0 mL of 1.0×10^{-3} M KTCl with a 1.0×10^{-3} M Na–TPB of solution. As is obvious from Figure 5 the amount of ketamine can be accurately determined from the end point of the titration curve.

Determination of KTCl in urine and pharmaceutical formulations

Ketamine hydrochloride was measured in biological fluids (urine) and pharmaceutical preparations (ampoules). Each sample was analyzed in triplicate, using this sensor by the standard addition and the calibration methods. It is noted, from Table 3, that the results were accurate and reproducible and the recovery of KTCl is almost quantitative.

The results of applying the above methods are compared with the values obtained from the official method [55]. F-test was used for comparing the precious of the two methods and t-test for comparing the accuracy. The calculated F-and t-test in Table 3 were less than critical (tabulated) ones. Thus, there is no significant difference between the precisions or the accuracies of the two methods at 95% confidence levels.

Conclusions

The proposed chemically modified carbon paste electrode based on a modifier namely Ketaminium tetraphenylborate (KT-TPB) as an electroactive ion exchanger complex might be a useful analytical tool and interesting alternative for the determination of KT ions in pharmaceutical preparations and urine samples. The electrode shows high sensitivity, reasonable selectivity, fast static response, wide pH range, concentration range 9.0×10^{-6} - 1.0×10^{-2} M, low detection limits of 7.3×10^{-6} M with minimal sample pretreatment.

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Figure captions

Fig. 1: Variation of electrode potentials with different plasticizers.

Fig. 2: Influence of pH on the response of the present electrode at 1.0×10^{-4} and 1.0×10^{-3} M

Fig. 3: Typical potential–time plot for response of KT-CMCPE

Fig. 4: Calibration graphs for KT-CMCPE at test solution temperature 25, 35, 45 and 55 ^{o}C

Fig. 5: Potentiometric titration curve of 5.0 mL $1.0\text{x}10^{-3}$ M solution KTCl with $1.0\text{x}10^{-3}$ M solution Na-TPB using the present electrode

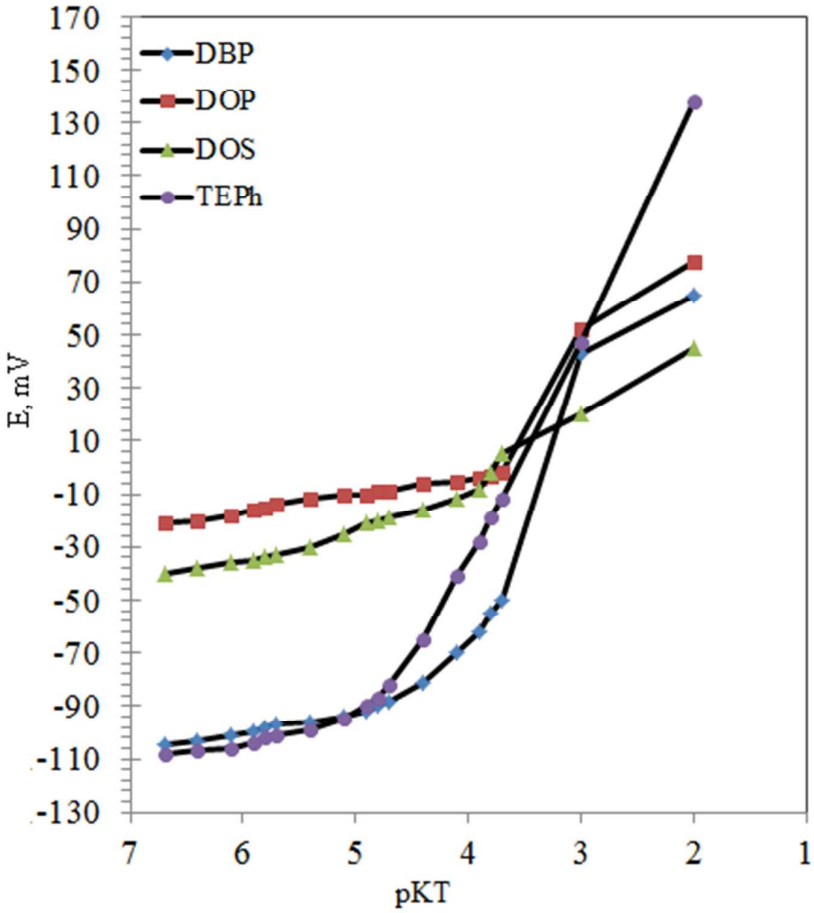

Fig. 1: Variation of electrode potentials with different plasticizers.

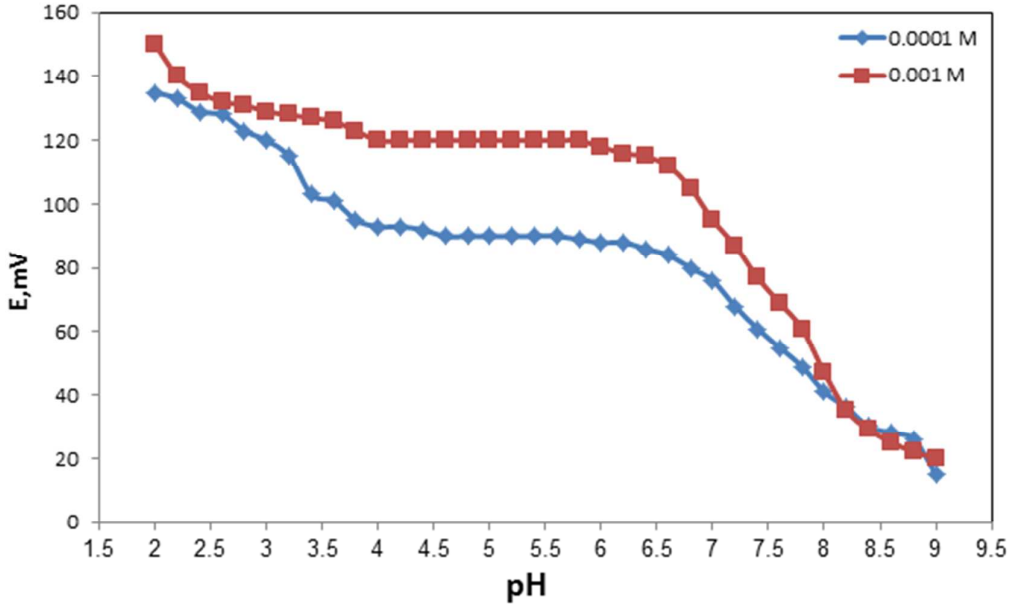

Fig. 2: Influence of pH on the response of the present electrode at 1.0×10^{-4} and 1.0×10^{-3} M

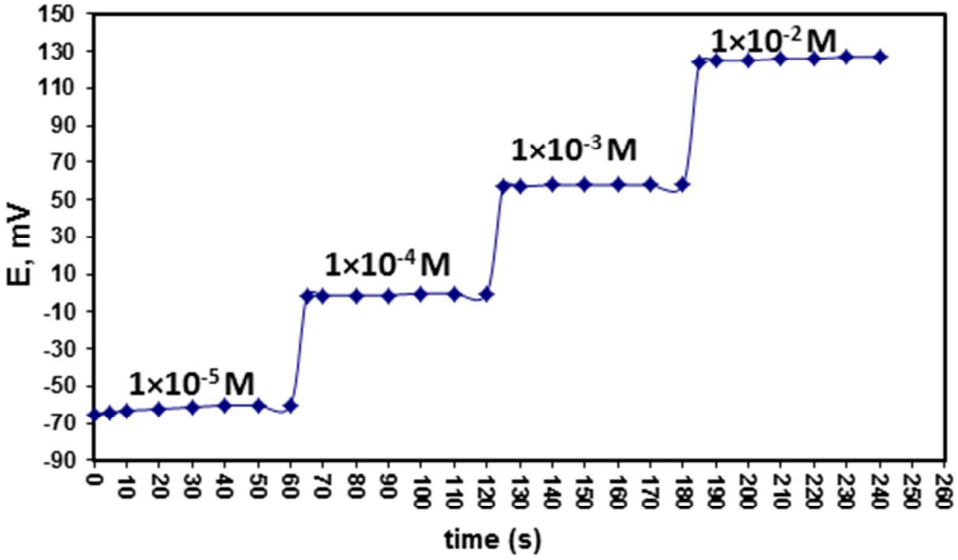

Fig. 3: Typical potential–time plot for response of KT-CMCPE

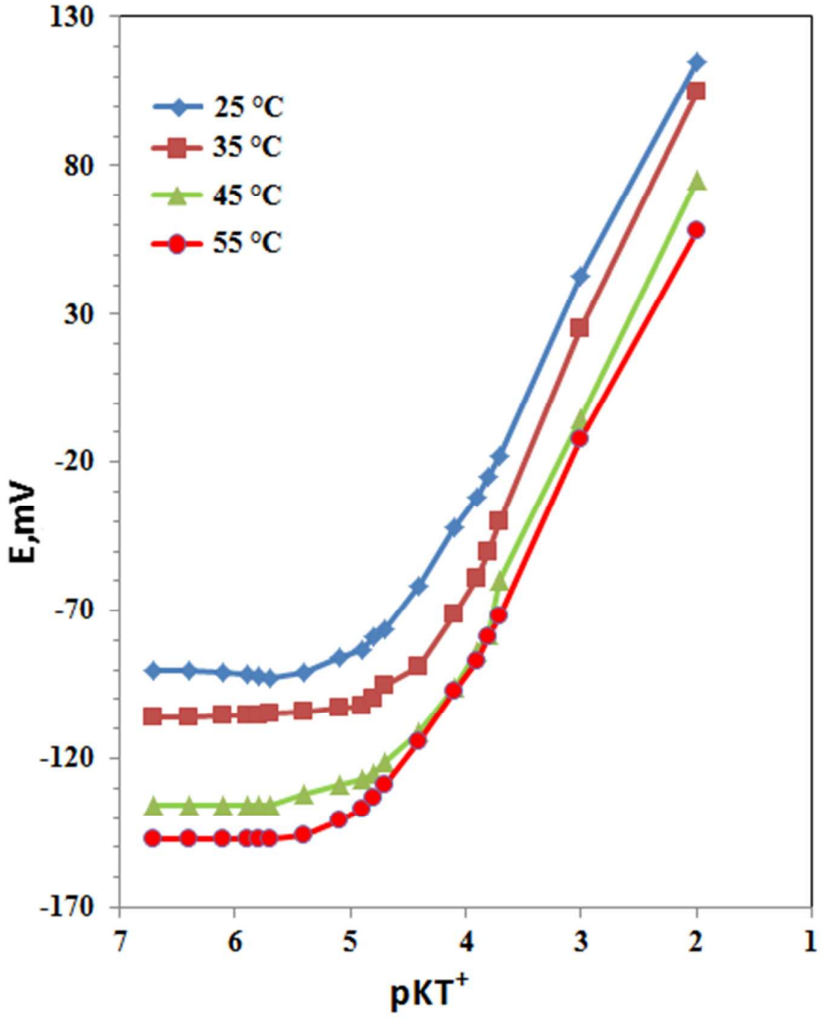

Fig. 4: Calibration graphs for KT-CMCPE at test solution temperature 25, 35, 45 and 55 °C

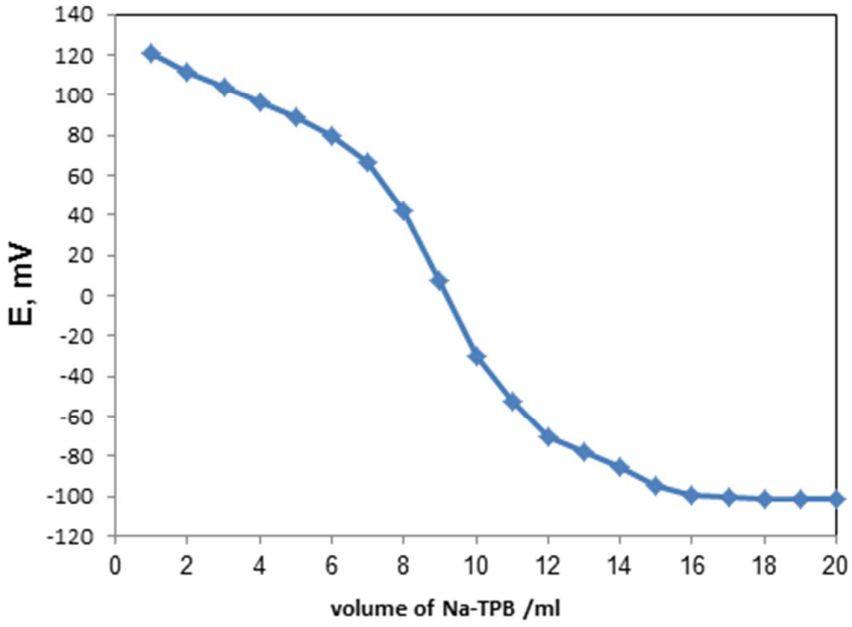

Fig. 5: Potentiometric titration curve of 5.0 mL $1.0x10^{-3}$ M solution KTCl with $1.0x10^{-3}$ M solution Na-TPB using the present electrode

Table 1: Composition and slope of calibration curve for KT-CMCPE at 25.0±0.1

	Ion Exchanger	Composition (%) g/p	I	g	p	A	Slope (mV/decade)	Linear Range (M)	Detection Limit(M)	R.S.D %	Response Time(s)
1	---	-	-	54.5	45.5 TEPh	-	24.7±0.3	9.0×10^{-5}-1.0×10^{-2}	7.8×10^{-5}	1.10	18
2	KT-TPB	1.20	0.1	54.5	45.2 TEPh	0.20	35.8±0.6	7.2×10^{-5} -1.0×10^{-2}	5.2×10^{-5}	1.12	9
3	KT-TPB	1.20	0.3	54.4	45.1 TEPh	0.20	38.2±0.5	5.3×10^{-5} -1.0×10^{-2}	2.7×10^{-5}	1.15	12
4	KT-TPB*	1.20	0.5	54.3	45.0 TEPh	0.20	58.9±0.3	9.0×10^{-6} -1.0×10^{-2}	7.3×10^{-6}	0.76	8
5	KT-TPB	1.20	0.5	54.3	45.2 TEPh	-	52.3±0.7	6.4×10^{-5} -1.0×10^{-2}	2.1×10^{-5}	0.84	15
6	KT-TPB	1.20	1.0	54.0	44.8 TEPh	0.20	45.2±0.5	1.9×10^{-5} -1.0×10^{-2}	1.0×10^{-5}	1.12	13
7	KT-TPB	1.20	1.5	53.7	44.6 TEPh	0.20	50.3±1.3	$3.6x10^{-5}$-$1.0x10^{-2}$	$1.4x10^{-5}$	0.77	9
8	KT-TPB	1.20	2.0	53.5	44.3 TEPh	0.20	41.8±0.9	$4.7x10^{-5}$-$1.0x10^{-2}$	$2.3x10^{-5}$	0.57	9
9	KT-TPB	1.20	3.0	52.8	44.0 TEPh	0.20	39.5±1.1	$7.4x10^{-5}$-$1.0x10^{-2}$	$4.0x10^{-5}$	0.77	10
10	KT-TPB	1.20	4.0	52.3	43.5 TEPh	0.20	34.3±0.5	$9.6x10^{-5}$-$1.0x10^{-2}$	$7.5x10^{-5}$	0.91	8
	Effect of different plastecizer										
11	KT-TPB	1.20	0.5	54.3	45.0 DPB	0.20	40.7±0.8	8.0×10^{-5}-1.0×10^{-2}	3.0×10^{-5}	1.10	12
12	KT-TPB	1.20	0.5	54.3	45.0 DOP	0.20	25.8±0.6	2.5×10^{-4} -1.0×10^{-2}	5.0×10^{-5}	1.10	10
13	KT-TPB	1.20	0.5	54.3	45.0 DOS	0.20	28.2±0.7	1.0×10^{-4}–1.0×10^{-2}	4.0×10^{-5}	1.05	11
	Effect of different ion pair										
14	KT -SM	1.20	0.5	54.3	45.0 TEPh	0.20	26.3±0.6	$6.0x10^{-5}$-$1.0x10^{-3}$	$2.3x10^{-5}$	0.92	10
15	KT -ST	1.20	0.5	54.3	45.0 TEPh	0.20	22.4±0.5	$4.7x10^{-5}$-$1.0x10^{-2}$	$1.5x10^{-5}$	1.05	12
16	KT -PM	1.20	0.5	54.3	45.0 TEPh	0.20	25.8±0.7	$2.5x10^{-4}$-$1.0x10^{-2}$	$9.2x10^{-5}$	0.84	9
17	KT- PT	1.20	0.5	54.3	45.0 TEPh	0.20	30.2±0.8	$3.5x10^{-5}$-$1.0x10^{-2}$	$1.0x10^{-5}$	0.72	11
18	KT- TPB*	1.20	0.5	54.3	45.0 TEPh	0.20	47.8±0.4	$2.0x10^{-5}$-$1.0x10^{-2}$	$9.0x10^{-6}$	0.57	8
	Different of g/p ratios										
19	KT-TPB	0.75	0.5	42.6	56.7 TEPh	0.20	42.1±0.7	2.4×10^{-5} –1.0×10^{-2}	1.0×10^{-5}	1.14	11
20		0.90	0.5	47.2	52.3 TEPh	0.20	43.9±0.2	2.6×10^{-5} –1.0×10^{-2}	9.2×10^{-6}	0.53	9
21		1.05	0.5	51.0	48.3 TEPh	0.20	45.3±0.5	3.0×10^{-5} –1.0×10^{-2}	9.0×10^{-6}	0.51	10
22		1.20	0.5	54.3	45.0 TEPh	0.20	58.9±0.3	9.0×10^{-6} –1.0×10^{-2}	7.0×10^{-6}	0.47	8
23		1.35	0.5	57.1	42.2 TEPh	0.20	42.0±0.7	4.5×10^{-5} –1.0×10^{-2}	1.7×10^{-5}	0.68	14

I: ion-exchanger g: graphite p: plasticizer R.S.D: Relative standard deviation

* selected composition A: additive Na-TPB

Table 2: Selectivity coefficients of various interfering ions for proposed electrode

Interfering ions	MPM	SSM
Na^{+}	1.45×10^{-4}	4.64×10^{-5}
K^{+}	2.80×10^{-4}	4.38×10^{-4}
Ag^{+}	1.88×10^{-4}	3.95×10^{-4}
Li^{+}	5.47×10^{-4}	7.61×10^{-5}
Cd^{++}	1.49×10^{-5}	8.62×10^{-4}
Ca^{++}	4.24×10^{-4}	2.18×10^{-4}
Ni^{++}	5.28×10^{-4}	3.80×10^{-4}
Co^{++}	2.01×10^{-4}	2.94×10^{-4}
Cu^{++}	1.65×10^{-5}	4.16×10^{-4}
Pb^{++}	5.45×10^{-4}	2.63×10^{-4}
Zn^{++}	4.21×10^{-4}	2.15×10^{-4}
Cr^{+++}	4.04×10^{-4}	2.00×10^{-4}
Ampicilline	1.23×10^{-4}	5.45×10^{-4}
Rocephen	1.87×10^{-3}	1.12×10^{-4}
Gentamycine	1.29×10^{-4}	2.95×10^{-3}
Lasix	5.21×10^{-4}	1.42×10^{-3}
Hydrocortisone	3.68×10^{-4}	4.78×10^{-4}
Diclofene	3.10×10^{-4}	5.24×10^{-4}
Glucose	4.86×10^{-5}	--
Galactose	6.24×10^{-4}	--
Fructose	1.68×10^{-5}	--
Sucrose	3.75×10^{-4}	--

Table 3: Analysis of KTCl in various samples using standard addition and calibration curve methods.

Samples		M		X %	R.S.D%	F-Value	t-Value
		Taken	Found				
Ampoule							
	C	1.00×10^{-5}	9.95×10^{-6}	99.50	1.06	2.36	3.01
		2.00×10^{-4}	1.95×10^{-4}	97.50	1.25	2.54	0.29
	S	1.00×10^{-5}	9.88×10^{-6}	98.80	2.10	3.21	3.14
		5.00×10^{-4}	4.92×10^{-4}	98.40	0.21	1.99	1.75
Urine							
	C	1.00×10^{-5}	9.85×10^{-6}	98.50	1.08	2.35	0.71
		2.00×10^{-4}	1.93×10^{-4}	98.75	0.24	2.19	1.86
	S	1.00×10^{-5}	1.02×10^{-5}	102.0	0.58	1.54	2.36
		5.00×10^{-4}	4.87×10^{-4}	97.40	0.42	1.43	2.35

C: calibration curve, S: standard addition method

R.S.D.: relative standard deviation X: recovery

The critical value of F=6.39 and the critical value of t=3.707.