Development of a New Coated Graphite Phenylephrine Potentiometric Sensor and Its Applications to Pharmaceutical and Biological Analysis

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Received: May 22, 2011
Accepted: September 9, 2011

Abstract
The construction and performance characteristics of a coated graphite phenylephrine-selective electrode based on incorporation of the ion-association complex of phenylephrine-tetraphenylborate in plasticized PVC matrix was studied. The electrode exhibited a Nernstian slope of 59.0 mV/decade to phenylephrine over a wide concentration range from 3.0×10^{-6} to 5.6×10^{-2} M with a low detection limit of 1.5×10^{-6} M. The proposed electrode manifested advantages of fast response, long life time and, most important, good selectivities for phenylephrine relative to a wide variety of common foreign inorganic cations, anions and also organic species. The electrode was successfully applied to determine phenylephrine in adult cold tablets, phenylephrine eye-drops and also blood serum samples. The inclusion complex formation between α- and β-cyclodextrine and phenylephrine was studied potentiometrically by the proposed electrode.

Keywords: Phenylephrine, Coated graphite electrode, Potentiometry, PVC membrane electrode, Pharmaceutical analysis

DOI: 10.1002/elan.201100281

1 Introduction

Phenylephrine (PE), (*R*)-3-[-1-hydroxy-2-(methylamino)ethyl]phenol (Figure 1), is a phenylalkylamine belonging to a group of stimulants which are sympathomimetic with mainly direct effects on adrenergic receptors [1,2]. PE is in a class of medications called nasal decongestants which work by reducing swelling of the blood vessels in the nasal passages without stimulating effects on the central nervous system [3]. PE-HCl and its salts are frequently included in preparations for the symptomatic relief of nasal congestion, cough and cold symptoms. It is present in the formulation of several vasopressor medicines, in eye washes, in nasal decongestant and in syrups.

The requirement of rigorous control of PE concentration in pharmaceutical industry and also biological samples had led to the development of a variety of determination methods such as liquid and gas chromatography [4–7], spectrophotometry [8,9], spectrofluorimetry [10,11] and electrochemistry [12–14]. However, most of these methods are either time-consuming or require expensive and sophisticated instruments, well controlled experimental conditions and some sample pretreatments. A conventional polymeric membrane electrode for PE has also been reported [15]. However, this electrode also suffered from some disadvantages such as limited linear range, near-Nernstian response and interferences of some inorganic and organic species which significantly limited its practical application.

Developments in pharmaceutical analysis with ion-selective electrodes (ISEs) have enabled the activity of various organic species of pharmaceutical interest to be measured directly and selectively and, in most instances, without prior separation of the active substance from the formulation matrix. Moreover, the pharmaceutical determinations based on ISEs are simple, rapid, of low cost, with a wide concentration range, precise and accurate and applicable to colored and turbid solutions [16]. These make ISEs a very attractive alternative tool for pharmaceutical analysis [17,18]. Thus, during the last three decades, many efforts have been focused on the introduction of different configuration of liquid membrane ISEs. Therefore, the configuration of liquid ISEs were changed from the conventional-type liquid membrane electrodes with an internal solution to wire type electrodes (WTEs), such as the coated wire electrodes (CWEs) [19]. In CWEs, new advantages are provided due to total elimination of internal filling solution which is a necessity in conventional-type liquid membrane electrodes. More simplicity of design, a smaller sample volume, more mechanical stability and the possibility of miniaturization and microfabrication are the important advantages which have spread the

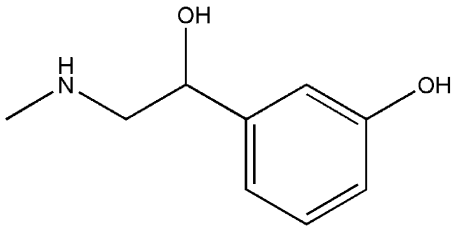

Fig. 1. The chemical structure of phenylephrine.

application of CWEs in pharmaceutical and biological analysis. Furthermore, these electrodes usually exhibit better selectivities and also lower detection limits than the conventional-type polymeric membrane electrodes [20,21].

With respect to importance of the determination of PE in pharmaceutical and clinical analysis, development of a potentiometric selective CWE with wide linear range and good selectivity for easy, fast and selective determination of PE can be very valuable. In this paper, the preparation, characterization and analytical application of a new membrane coated graphite electrode (CGE) in pharmaceutical preparations and also biological matrices have been described. The membrane used in the CGE was made from PE-TPB ion association complex as an ion exchanger. The obtained results showed that the constructed CWE exhibited a very good detection limit and also excellent selectivity to PE which permit direct determination of this drug concentration in different media without prior separation steps.

2 Experimental

2.1 Reagents

All of the chemical used were of highest purity available and used without any further purification except for vacuum drying. Doubly distilled water was used throughout for preparing all aqueous solutions. Reagent grade *o*-nitrophenyl octyl ether (NPOE), dibuthyl phthalate (DBP), diocty phthalate (DOP), dioctyl sebacate (DOS), dibutyl sebacate (DBS), sodium tetraphenyl borate (NaTPB), potassium tetrakis(*p*-chlorophenyl)borate (KT*p*ClPB), tetrahydrofuran (THF), high relative molecular weight PVC, nitrate salts of all cations and also potassium salts of all anions (all from Merck) were used as received. Phenylepherine hydrochloride (PE-HCl) was obtained from Damavand Darou Mfg. Company, Damghan, Iran. Blood serum samples were obtained from healthy volunteers. A working standard solution of 0.2 M was prepared by dissolving 0.4074 gr of PE-HCl in water in a 10 mL calibrated volumetric flask. More dilute solutions were prepared by further dilution of appropriate volumes of the standard solution with water. The pH adjustments were made with either dilute hydrochloric acid or potassium hydroxide solution as required.

The PE-TPB ion exchanger was prepared by mixing an equal volume of a 10^{-2} M aqueous solution of PE-HCl and NaTPB. The resulting precipitate was filtered through a filter paper, thoroughly washed with distilled water and dried under a vacuum over P_2O_5.

2.2 Preparation of the Electrode

The general procedure to prepare the PVC membranes was to dissolve various amounts of ionophore, additive KT*p*ClPB and powdered high molecular weight PVC in 5 mL THF. To these, appropriate amount of plasticizers were added. Then, the mixture was shaken vigorously. The resulting solution was evaporated slowly at ambient temperature until an oily concentrated solution was obtained.

Spectroscopic grade graphite rods (2 mm diameter) were used for the construction of CGEs. A shielded copper wire was glued to one end on the graphite rod, and then the graphite rode was sealed into the end of a PVC tube of about the same diameter with epoxy resin. The working surface of the electrode was polished with fine alumina slurries on a polishing cloth, sonicated in distilled water and dried in air. The polished graphite electrode was dipped into the membrane solution mentioned above, and the solvent was evaporated. A membrane was formed on the graphite surface, and the electrode was allowed to stabilize overnight. The electrode was finally conditioned by soaking in a 1.0×10^{-2} M solution of PE-HCl for 8 h. An unmodified polished graphite electrode was also tested for comparative purposes, and found that it did not show any potentiometric response to PE-HCl solutions, after the conditioning period.

2.3 Emf Measurements

All potentiometric measurements with the CGE were carried out with the following cell assembly

Ag|AgCl (satd)|test solution|membrane|graphite surface

The emf observations were made relative to a double-junction silver/silver chloride electrode containing a saturated solution of KCl (Metrohm) with the chamber filled with potassium nitrate solution. Suitable increments of PE-HCl solution were added to 20 mL of 0.05 M acetate buffer solution to cover the concentration range 1.0×10^{-6} to 1.0×10^{-1} M and the emf values were recorded after each addition. Calibration graphs were then constructed by plotting the recorded potentials versus log [PE]. The obtained graphs were employed for the characterization of the CGE.

2.4 Potentiometric Assay of Pharmaceutical Preparations

Two finely powdered tablets (5 mg/tablet) or 2 mL of eye drop (500 mg/100 mL) was transferred with 0.05 M acetate buffer solution (pH 5) into a 50 mL calibrated flask.

Table 1. Optimization of membrane ingredients.

No.	Composition (%)				Slope (mV/decade)	Linear range (M)
	PVC	Plasticizer	Ionophore	KT*p*ClPB		
1	32.3	DOP, 64.7	3.5	0.0	35.8	2.2×10^{-5}–3.0×10^{-2}
2	32.0	DOP, 64.0	4.0	0.0	43.2	5.0×10^{-6}–3.0×10^{-2}
3	31.8	DOP, 63.7	4.5	0.0	39.4	3.7×10^{-5}–1.0×10^{-2}
4	31.8	NPOE, 63.7	4.0	0.0	42.1	7.5×10^{-6}–3.0×10^{-2}
5	31.5	DOP, 63.0	4.0	1.5	55.2	3.0×10^{-6}–2.1×10^{-2}
6	31.5	DOP, 62.7	4.0	1.8	59.0	3.0×10^{-6}–5.6×10^{-2}
7	31.5	NPOE, 62.7	4.0	1.8	53.8	5.0×10^{-6}–3.0×10^{-2}
8	31.5	DOS, 62.7	4.0	1.8	49.1	1.2×10^{-5}–3.0×10^{-2}
9	31.5	DBS, 62.7	4.0	1.8	45.9	2.2×10^{-5}–2.1×10^{-2}
10	31.5	DBP, 62.7	4.0	1.8	55.2	7.5×10^{-6}–3.0×10^{-2}

The solution was diluted to the mark with buffer, shaken for 5 min and then 20 mL of the obtained solution was transferred into a 50 mL beaker. The PE content of the solution was then determined by the proposed CGE, using the calibration graph.

2.5 Recovery of PE from Human Blood Serum Sample

Aliquots of 5 mL human blood serum were transferred to a 50 mL calibrated flask, made up to the mark with 0.05 M acetate buffer solution (pH 5) and shaken for 5 min. 20 mL of this solution was transferred into a 50 mL beaker. Different amounts of PE were spiked into the beaker solution separately, and then PE content of the solution was determined by the proposed CGE, using standard addition method.

3 Results and Discussion

3.1 Optimization of Membrane Components

The sensitivity, selectivity and linearity of the ion selective electrodes depend on the type and amount of ionophores and also significantly on the membrane composition, the properties of plasticizers and additive used [22–26]. Since the nature of plasticizer influences the dielectric constant of the membrane phase and the mobility of the ionophore molecules [24,25], it was expected to play a key role in the determination of the ion selective electrode characteristics. Thus, the effect of membrane composition, the nature and amount of the plasticizer (DBS, DOS, DBP, NPOE and DOP) and additives on the potential response of the PE-selective electrode were investigated and the results were summarized in Table 1. As seen from Table 1, among five plasticizers examined, DOP resulted in the best sensitivity and linear range. Moreover, 4% of ion exchanger was chosen as the optimum amount in the PVC membrane (No. 6). A further addition of ion exchanger, however resulted in some decreases in the response of the electrode, most probably due to some inhomogeneities and possible saturation of the membrane [27]. The high amount of the ionophore may also induced strong interactions between polymeric chains and the ionophore, preventing mobility of the segments as explained by Hall considering experimental observations of Reinhoudt et al. [28].

In general, the thickness and hardness of the membrane depend on the amount of PVC used. At high PVC content, the membrane becomes too dense, which makes the transport of cations into the membrane more difficult and results in increased resistance. On the other hand, at low PVC content, the membrane becomes mechanically weak and swells up easily in aqueous solution. A plasticizer/PVC ratio of 2 was chosen as the optimum amount in the PVC membrane.

It is well known that potentiometric membrane selective electrodes in most cases require the addition of a lipophilic additive in the membrane composition [24,29], so that without such additives many electrodes do not respond properly. The presence of such lipophilic additives in selective membrane electrodes not only diminishes the ohmic resistance [29] and enhances the response behavior, selectivity and sensitivity of the membrane electrodes [30–32], but also may catalyze the exchange kinetics at the sample-membrane interface [32]. Their main role is attributed to the inducing permselectivity to some PVC membrane selective electrodes [29,33]. As can be seen in Table 1, in the absence of additive, the proposed electrode did not show Nernstian response characteristics (No. 2). However, addition of 1.8 mg KT*p*ClPB as a suitable additive enhanced the slope of the calibration curve from a low value of 43.2 (No. 2) to a Nernstian slope of 59.0 mV/decade over a wider concentration range potential response (No. 6).

3.2 Response Characteristics of the Phenylephrine-Selective Electrode

Before use, the liquid membrane electrode must be conditioned by soaking in a PE-HCl ion solution in order to ensure the equilibrium at the membrane–water interface. Optimum conditioning time for the proposed CGE in a 1.0×10^{-2} M PE-HCl solution was found to be 8 h. The conditioned electrodes then generated stable potentials when placed in contact with PE-HCl solutions.

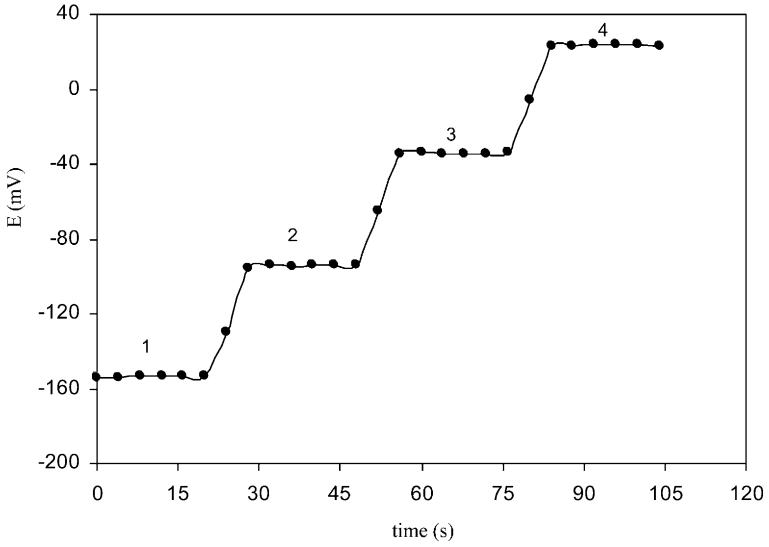

Fig. 2. Dynamic response time of the PE-selective CGE for step wise addition of PE-HCl concentration (M): (1) 1×10^{-5}; (2) 1×10^{-4}; (3) 1×10^{-3}; (4) 1×10^{-2}.

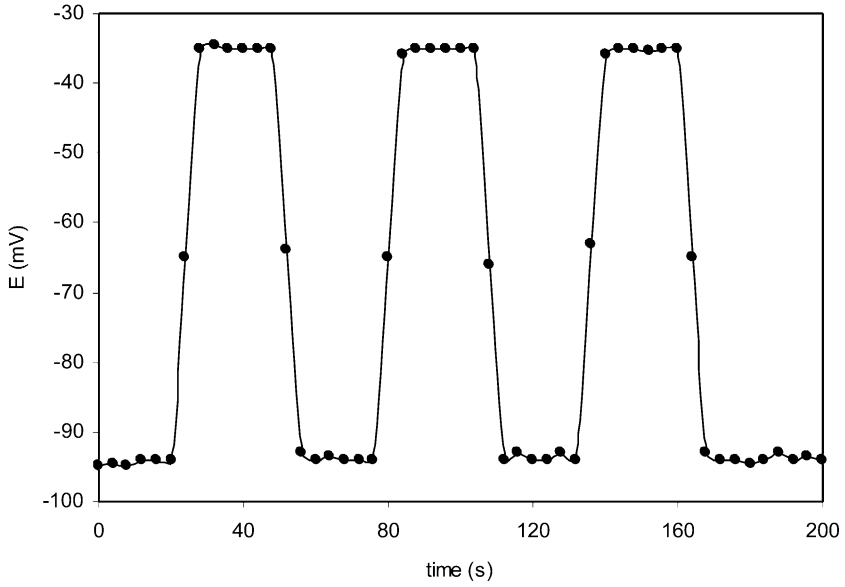

Fig. 3. Dynamic response characteristics of CGE for several high-to-low cycles.

The average time required for the membrane sensor to reach a potential within ±1 mV of the final equilibrium value after successive immersion of a series of PE-HCl solutions, each having 10-fold difference in concentration, was less than 8 s over the entire concentration range (Figure 2) and the potentials stayed constant after this time.

The standard deviation of the reading potential responses every 10 min over a period of 3 h in a 1.0×10^{-3} M of PE-HCl solution was obtained 0.5 mV ($n=18$) that revealed good stability of potential responses of the proposed electrode. Moreover, the potential reading for the electrode dipped alternatively into stirred solutions of 1.0×10^{-3} and 1.0×10^{-4} M of PE-HCl (Figure 3) represented a standard deviation of 0.6 mV ($n=8$). This very low standard deviation showed good reversibility of the coated graphite PE-selective electrode.

The lifetime of an ion-selective electrode is usually defined as the time interval between the conditioning of the membrane and the moment when at least one of its response characteristics changes. The relative lifetime of the proposed PE-selective electrode was studied by periodically obtaining the slope and linear range of the calibration curve over the range of 5.0×10^{-7} to 5.6×10^{-2} M PE-HCl solutions during two months. Before each measurement, the electrode was conditioned in a 1.0×10^{-2} M PE-HCl solution. The experimental results showed that the lifetime of the PE-selective electrode was more than

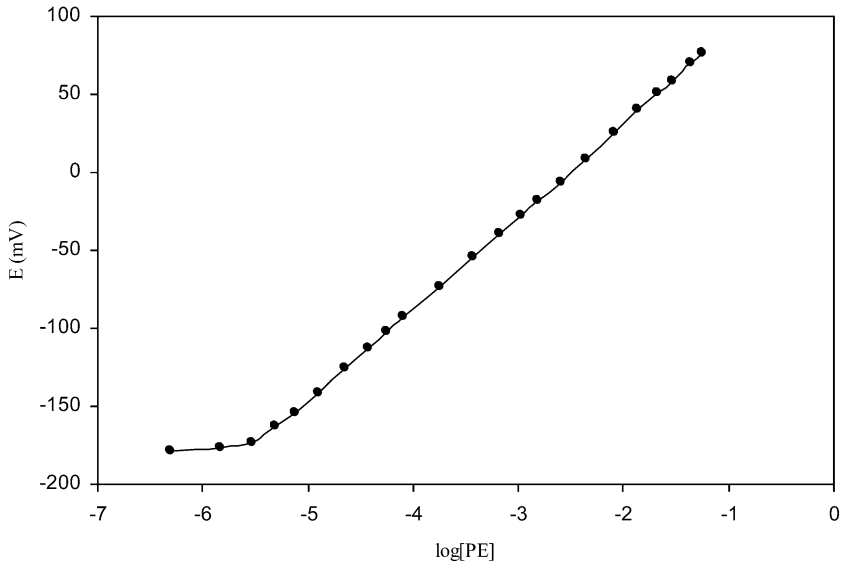

Fig. 4. Calibration graph for the CGE under optimum conditions.

2 months. During this time the detection limit and slope of the electrodes remained almost constant.

The emf responses of the proposed PE-ISE based on the PE-TPB ion pair (prepared under optimal membrane ingredients) at varying concentrations of PE-HCl (Figure 4) indicated a linear range from 3.0×10^{-6} to 5.6×10^{-2} M with a Nernstian slope of 59.0 ± 0.3 mV/decade ($n=6$) of PE-HCl concentration. The limit of detection, as determined from the intersection of two extrapolated segments of the calibration graph, was 1.5×10^{-6} M.

3.3 Effect of pH

The pH dependence of the potential response of the proposed CGE at 1.0×10^{-4} M PE-HCl solution in the pH range of 2–10 was tested and the results were shown in Figure 5. As can be seen, the electrode potential was independent of pH in the range of 3.5–8.0. This can be taken as the working pH range of the electrode. At lower pH values potential decreased because the PE-TPB ion pair complex in the membrane of electrode was unstable in this medium [34]. On the other hand, decrease in potentials above pH 8.0 would be presumably due to the formation of the deprotonated PE species (pK_a value of PE is 8.9) and gradually increasing the free form of PE base in the test solution which was not sensed by the CGE electrode.

3.4 Effect of Partially Nonaqueous Media on the Electrode

Sometimes the sample may contain non-aqueous content in order to dissolve the ingredients, and so it is necessary the selective electrode also works well in such partially

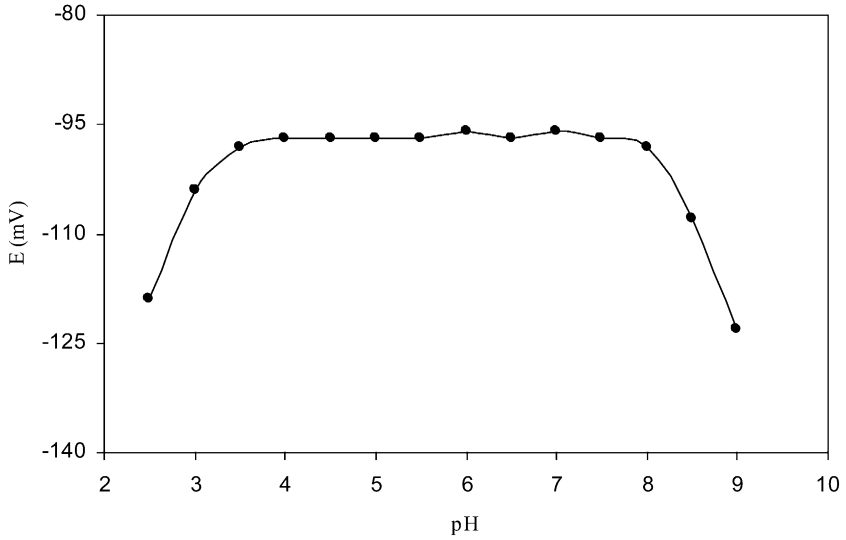

Fig. 5. Effect of pH of the test solution (1.0×10^{-4} M) on the potential response of the PE-selective CGE.

Table 2. Effect of partially nonaqueous media on the response of coated graphite PE-selective electrode.

Nonaqueous content (% v/v)	Slope (mV/decade)	Linear range (M)
0	59.0	3.0×10^{-6}–5.6×10^{-2}
Methanol		
10	58.1	5.0×10^{-6}–1.3×10^{-2}
20	56.9	5.0×10^{-6}–8.2×10^{-3}
Ethanol		
10	58.0	5.0×10^{-6}–1.3×10^{-2}
20	56.6	7.5×10^{-6}–8.2×10^{-3}
Acetone		
10	57.4	7.5×10^{-6}–1.3×10^{-2}
20	56.2	5.0×10^{-6}–8.7×10^{-2}

non-aqueous media. Thus, the performance of the proposed CGE was also investigated in partially non-aqueous media using methanol, ethanol, and acetone mixtures with water. The calibration plot of the electrode was obtained in the different mixture (v/v) of ethanol-water, methanol-water and acetone-water. The data were summarized in Table 2. From the data obtained, it was concluded that the CGE worked satisfactorily in solutions having a maximum of 20% (v/v) non-aqueous content. In these mixtures the working concentration range and slope remained almost unaffected, and only a little decrease was observed (Table 2). Therefore, the electrode functioned well in the presence of up to 20% nonaqueous content. However, above 20% nonaqueous content, the slope and working concentration range were reduced, and the potentials showed drift more probably due to leaching of the membrane ingredients into the solution and so caused a significant interference in the electrode functioning.

3.5 Potentiometric Selectivity Coefficients

The selectivity behavior is the most important characteristic of an ion selective electrode as it determines the applicability of any sensor in the presence of foreign ions in the samples. Selectivity interprets relative electrode response for the primary ion (A) over other species (B) present in solution, which is usually expressed in terms of potentiometric selectivity coefficient ($K_{A,B}^{pot}$). The potentiometric selectivity coefficients were determined by the fixed interference method (FIM) [35,36] at 1.0×10^{-3} M concentration of the interfering species. The resulting selectivity coefficients obtained for the proposed PE-selective CGE were listed in Table 3. From the data given in Table 3, it is revealed that the proposed CGE has good selectivity toward PE with respect to a lot of cations, anions and also biological materials. So, the disturbance produced by these species is negligible in the determination process of PE in different samples.

In Table 4, analytical performance of the proposed CGE was compared with the corresponding values previously reported for usual polymeric membrane PE-selective electrodes [15,37]. As seen, the proposed CGE showed superior, in most cases, response characteristics and selectivity behavior to the previous polymeric membrane PE-selective electrodes. These improvements can be attributed to the effect of inherent characteristics of CGE, which usually has better detection limit and selectivity coefficients with respect to the similar usual polymeric membrane electrodes [20,26], and also use of a suitable ionic additive (KT*p*ClPB) to increase the permselectivity of the membrane. It should be noted that lack of internal solution and more mechanical stability are further advantages of the proposed CGE over the usual liquid membrane selective electrodes. Moreover, the linear range of the proposed CGE (3.0×10^{-6}–5.6×10^{-2} M) is also comparable with some of other PE determination methods such as spectrophotometry [9] or electrochemistry [14] which have linear range 9.8×10^{-6}–2.5×10^{-4} M and 1.0×10^{-5}–5.0×10^{-3} M, respectively.

3.6 Analytical Applications

The proposed PE-selective CGE was found to work under laboratory conditions. It was successfully used as an indicator electrode in potentiometric titration of 20.0 mL of 1.0×10^{-3} M PE-HCl with a 5.0×10^{-2} M TPB solution. The resulting titration curve was shown in Figure 6. As can be seen, the titration curve has a distinct and accurate equivalent point and so the amount of PE

Table 3. Selectivity coefficients (log $k_{PE,I}^{pot}$) of various interfering species for the proposed CGE.

Interferent	log $k_{PE,I}^{pot}$
Li^+	−2.9
Na^+	−2.7
K^+	−2.8
Mg^{2+}	−3.4
Ca^{2+}	−3.7
Zn^{2+}	−3.1
Co^{2+}	−3.3
Cu^{2+}	−3.8
Fe^{3+}	−3.2
Ni^{2+}	−3.4
F^-	−3.1
Cl^-	−2.7
PO_4^{3-}	−4.1
HCO_3^-	−2.3
Urea	−2.1
Glocose	−2.5
Lactose	−2.6
Cytidine	−2.8
Glycine	−2.8
Ascorbic acid	−2.1
Tartaric acid	−2.2
Lactic acid	−3.1
Oxalic acid	−3.5
Ephedrine	−1.5
Trimazoline	−2.5
Naphazoline	−1.9
Paracetamol	−2.3
Chlorpheniramine maleate	−2.1

Table 4. Comparison of the potentiometric characteristics of the CGE and the previous reported PE-selective electrodes.

	CGE	Ref. [15]	Ref.[37]
Linear range (M)	3.0×10^{-6}–5.6×10^{-2}	1.5×10^{-4}–1.0×10^{-1}	1.0×10^{-5}–1.0×10^{-1}
Detection limit (M)	1.5×10^{-6}	–	8.9×10^{-6}
Slope (mV/decade)	59.0 ± 0.3	58.1 ± 0.6	57.5
Response time (s)	8	5	12
pH range	3.5–8.0	2.9–8.0	3.5–8.0

concentration can be accurately determined by the proposed electrode.

The proposed CGE also proved to be useful for the assay of PE content of pharmaceutical preparations. It was used to determine the PE content in adult cold tablet (5 mg/tablet) and eye drop (500 mg/100 mL). The results obtained from three replicate measurements were found to be 4.9 ± 0.3 mg/tablet and 491 ± 1.2 mg/100 mL for adult cold tablet and eye drop, respectively which were in satisfactory agreement with the declared amounts. The agreement is indicative of noninterference of the other ingredients and the excepients which are present in the formulations.

Moreover, in order to investigate the applicability of the proposed CGE to the determination of PE in the biological fluids, it was applied to the recovery of PE from human blood serum sample (prepared from clinical laboratory) as a good matrix. Different amounts of PE-HCl were spiked into the human blood serum sample and the PE contents were measured by standard addition method. The results were summarized in Table 5. As seen, the recoveries are quantitative at the various PE-HCl concentrations tested which revealed the proposed CGE can be applied for determination of PE concentration with satisfactory accuracy in biological matrices.

3.7 Complexation Reaction Between Phenylephrine and Cyclodextrines

Cyclodextrins (CDs) are cyclic oligosaccharides which have recently been recognized as useful pharmaceutical excipients. The molecular structure of these glucose derivatives generates a hydrophilic exterior surface and a nonpolar cavity interior. Thus, cyclodextrins can interact with drug molecules which lead to the formation of inclusion complexes. Such molecular encapsulation will affect many of the physicochemical properties of drugs, such as increase the aqueous solubility and rate of dissolution of poorly water-soluble drugs, increase the drugs stability, reduce or prevent gastrointestinal or ocular irritation, reduce or eliminate unpleasant smells or tastes, prevent drug-drug or drug-additive interactions and conversion oils and liquid drugs into microcrystalline or amorphous powders [38].

Table 5. Determination of PE ($\mu g\,mL^{-1}$) in blood serum.

Added	Found [a]	Recovery (%)
0	0	–
2.50	2.47 ± 0.3	98.8
25.00	24.60 ± 0.5	98.2
200.00	203.60 ± 0.8	101.8

[a] Average value of three replicate measurements

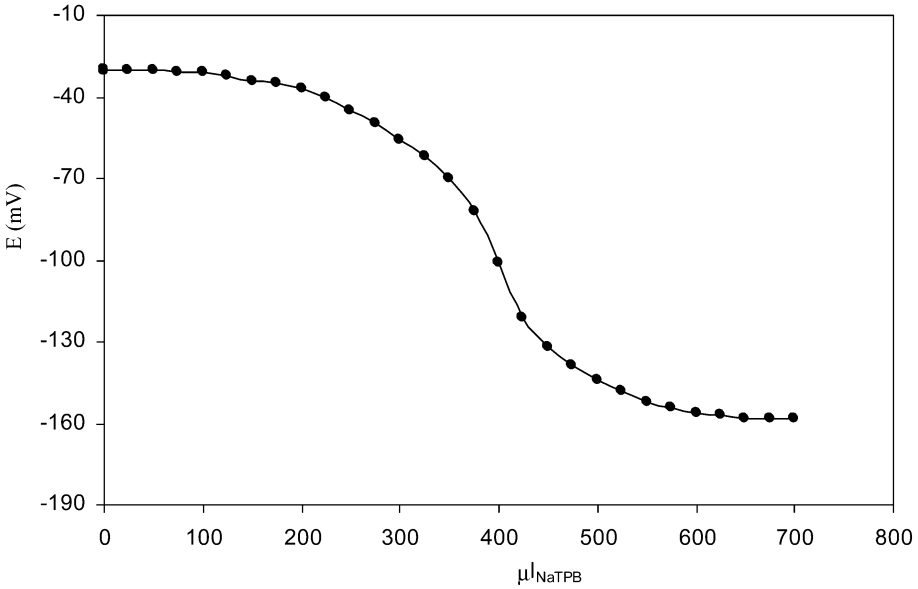

Fig. 6. Potentiometric titration curve of 20 mL of 1.0×10^{-3} M PE-HCl with 5.0×10^{-2} M NaTPB.

Several techniques were reported for characterization of the CDs and drugs inclusion complex such as chromatography, polarography, spectroscopy and polarimetry [38]. However, these techniques are time consuming, expensive and need sophisticated instruments. Potentiometry with ion selective electrodes can be a fast, cheap and easy technique to investigate the inclusion complexes of CDs with drugs. Thus, the proposed CGE was applied to evaluate the equilibrium constant of α- and β-CD-PE inclusion complexes:

$$\mathrm{PE} + \mathrm{CD} \overset{k_s}{\longleftrightarrow} \mathrm{Inclusion\ Complex}$$

The response of the CGE in the absence and presence of α- and β-CD (0.01 M) were shown in Figure 7. As seen, in the presence of CDs, the slop and linear range of the CGE calibration curve (Figure 7) were changed which indicated complex formation between these CDs and PE.

The data were investigated by first assuming a 1:1 equilibrium exists between CDs and PE. Thus, the equilibrium concentration constant, K_s, can be evaluated from the emf data using the classical Hildebrand equation [39,40] in the following form:

$$v^{-1} = (K_s m_1)^{-1} + 1$$

Where v is the concentration of PE complex with CD over its total concentration and m_1 is the free drug concentration. In Figure 7, for each potential value on Y axis, the corresponding value on X axis is free and total concentration of PE on calibration graph without (graph 1) and with CD (graph 2 or 3), respectively. If the free concentration was subtracted from the total concentration, the reminder should be the concentration of PE complex with CD. The plots of $1/v$ versus $1/m_1$ for the data involving PE inclusion complex with α- and β-CD were shown in Figure 8.

The plots were quite linear which confirmed the 1:1 stoichiometry of the inclusion complexes. The binding constant obtained for the PE complexes with α- and β-CD were 142 and 335, respectively. In order to show the suitability of the CGE sensor for binding constant studies, K_s was also calculated by spectrophotometric method based on the Benesi–Hildebrand equation [41]. The calculated K_s values (134 and 330 for the PE complexes with α- and β-CD, respectively) were in satisfactory agreement with those obtained with the proposed CGE sensor.

4 Conclusions

The PE-selective CGE based on ion association complex of PE-TPB exhibited appropriate analytical characteristics for the direct, easy and selective determination of PE in pharmaceutical and biological samples. A PE concentration as low as 3.0×10^{-6} M can be determined by the proposed electrode. The electrode showed good sensitivity, a low detection limit, long-term stability and applicability over a wide pH range. The electrode characteristics such as linear range, detection limit, life and response time and specially selectivity are comparable to the other usual polymeric membrane electrodes with an internal solution previously reported. Moreover, compared with other analytical methods such as GC, HPLC, spectrophotometry and spectrofluorimetry, which require expensive instrumentation and adequate sample preparation, the proposed electrode is inexpensive, highly selective, simple and easy to use.

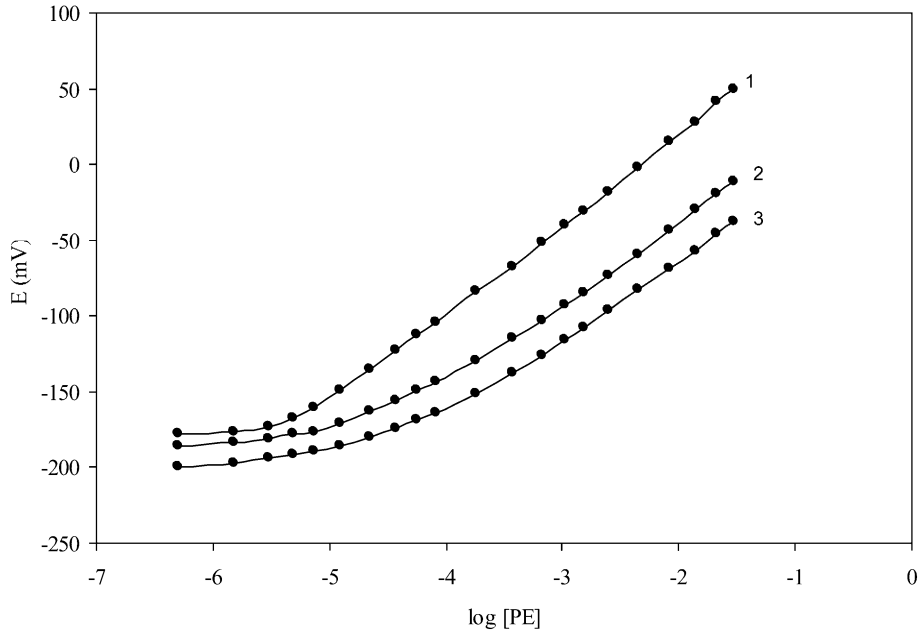

Fig. 7. Potential response of the PE-selective electrode without (1) and with α-CD (2) and β-CD (3).

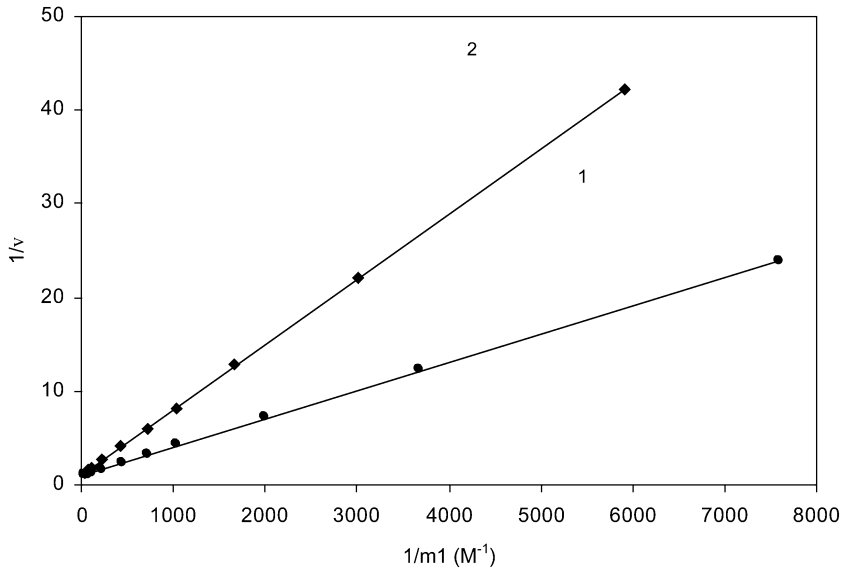

Fig. 8. Plots of $1/v$ versus $1/m_1$ for PE binding to β-CD (1) and α-CD (2).

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