Int. J. Electrochem. Sci., 14 **(2019)** 7437 – 7449, doi: 10.20964/2019.08.73

International Journal of
ELECTROCHEMICAL
SCIENCE
www.electrochemsci.org

A Compact-Cell Sensor based on Diazacrown Ether Derivative for the Determination of Ephedrine

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Received: 13 February 2019 / *Accepted:* 13 May 2019 / *Published:* 30 June 2019

In this study, a compact-cell sensor based on a plastic-membrane was introduced for the determination of ephedrine (EP) in pharmaceutical formulations. The sensing membrane of the sensor cell was made of either potassium tetrafluorophenyl borate (type-I) or N, N-bis-ethoxycarbony-1,4,7,10,13,16-hexaoxacyclooctadecane (type-II). The developed sensor exhibited typical Nernstian response (59.8 mV/decade) and high sensitivity (pM 6.2). The sensor was found to work in a pH range of 3.1–8.96 and showed good selectivity for EP relative to other organic and inorganic interferent. The sensor was applied effectively for the assessment of EP in different pharmaceutical formulations.

Keywords: Ephedrine, compact cell sensor, PVC membrane electrode.

1. INTRODUCTION

Ephedrine (EP) (Figure 1a) is chemically expressed as (C_6H_5.CH (OH).CH ($NHCH_3$).CH_3.1/2H_2O). It is a sympathomimetic amine that resembles adrenaline and amphetamine in its action and used as a medication and stimulant [1]. Its main medical use is in preventing low blood pressure during spinal anesthesia. The administration of EP by the oral rout at therapeutic doses results in the contraction of the peripheral vessels, thus it is used for the treatment of high blood pressure. It is used for the medication of asthma, narcolepsy obesity and nasal congestion. It causes the contraction of the sphincter but the relaxation of the detrusor muscle of the bladder, dilation of the pupil, and stimulation the central nervous system. The prolonged administration of EP has no cumulative adverse effect, but tolerance against the drug dosage develop over time.

There are many methods to determine ephedrine concentration and, among them, chromatographic methods are widely used. Yehia and Essam [2] applied a HPLC method to the analysis of a pharmaceutical formulations containing phenylephrine hydrochloride, paracetamol, ephedrine hydrochloride, guaifenesin, doxylamine succinate, and dextromethorphan hydrobromide. It was developed by a Kinetex® C18 column as a core-shell stationary phase with a gradient profile using acetonitrile at pH5. The proposed method had RSD% of <3% and the DL was < 2.0 μg/mL.

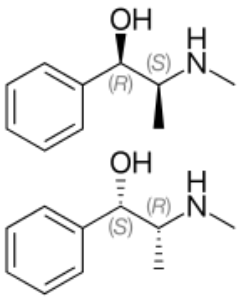
Tircova and Kozlik [3] developed a method including hydrophilic interaction LC with tandem MS- detection for EP in a pharmaceutical solid dosage form.

Xu and Yan [4] determined the metabolites of ephedrine and 4-hydroxyephedrine by LC-MS-MS method in rat urine and excretion profiles after oral administration of *Ephedra sinica* Stapf.

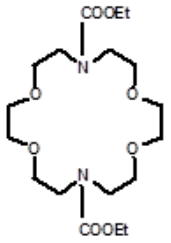
Other methods were also used for EP determination like spectrophotometric [5–7]. Recently, Mostafa et al [8] applied a smart spectrophotometric method to quantify EP without interference from coloring matter in a massive preparation. DeMarco and Mecarelli [9] applied a polarographic method for EP-determination.

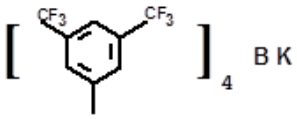
All of the above-mentioned methods have been applied successfully for the determination of EP. However, most of them were available only for bench-top measurements. In addition, they all require highly expensive instruments, chemicals, and trained chemists to obtain accurate results. These problems can be solved by the electrochemical sensors. They are characterized by fast response, easy to use, sensitive, low-cost, and do not need sample treatment. Some conventional types of ISE have been used for EP-determination. Bagheri et al [10] developed MIP sensor for the determination of EP. It was based on an Fe_3O_4@SiO_2@titanium dioxide-MIP nanocomposite. The LOD for EP was 0.0036 μmol L^{-1} (RSD <1.4%) and the linear range was 0.0090–2.8 μmol L^{-1} (RSD <1.6%). Cookeas and Efstathiou [11] applied an amperometric method for EP using a cobalt phthalocyanine modified carbon paste electrode. Kuchkarev et al [12] applied ion-selective electrodes based on liquid ion-exchangers, while PVC-matrix was used by Zareh et al [13] for the determination of EP.

The wide use of EP requires a tool for its easy and direct assessment and monitoring. The electrochemical sensors have been upgraded to a new generation of the compact-cell (CC). The first CC was prepared for ascorbic acid by Zareh [14]. Here, an original EP-CC sensor is introduced for the fast and direct determination of EP. It is established by the use of an original sensor made of synthesized N, N-bis-ethoxycarbonyl,10-diaza- 1,4,7,10,13,16-hexaoxacyclooctadecane. Figure 1, shows the structure formulas of all the used compounds.



(a)





(b) (c)

Figure 1. Structural formulas of ephedrine (EP) (a), *N, N-bis*-ethoxycarbonyl-1,10-diaza-4,7,13,16-tetraoxacyclo-octadecane (DZCE) (b) and potassium tetra-*kis*-[3,5-bis-(trifloro-methyl)-phenyl] borate (KTFPB) (c).

2. EXPERIMENTAL

2.1. Equipment

The cell-EMF values were measured using a bench top pH-meter (Jenway, UK) attached to a computer system. Spectrophotometric measurements were carried using a flow-injection spectrophotometer (UV1800-Shimadzu, Japan).

2.2. Chemicals and reagents

The following chemicals were used for the preparation of the EP-membrane for the EP-CC: tetrahydrofuran (THF) (Merck, Darstadt, Germany) (after distillation), didecyl phthalate (DDP) and potassium tetra-*kis*-[3,5-*bis*-(trifluoromethyl)phenyl]borate (KTFPB) (Sigma-Aldrich Chemie GmbH, Taufkirchen, Germany). The high molecular weight poly (vinyl chloride) (PVC) (Sigma-Aldrich Chemie) was used for the preparation of all membranes. The host molecule (DZCE) *N,Ń-bis*-ethoxycarbonyl,10-diaza-4,7,13,16-tetraoxacyclo-octadecane (diaza-18-crown-6) was kindly provided by E. Malinowska (Warsaw Technical University, Poland), which was synthesized according to the procedure described previously [15]. Ephedrine HCl, quinine, dopamine, caffeine, and pilocarpine hydrochloride were obtained from Sigma, while glycine, arginine, and sodium glutamate were procured from Aldrich. Nitrate salts of inorganic cations (Na^+, K^+, Li^+, NH_4^+, Ca^{++}, Mg^{++} and Ba^{++}) were purchased from (Panreac, Barcelona, Spain). Calculated amounts of 0.1 M and 0.01 M EP-solutions were used for preparing further diluted solutions (9.09×10^{-3} to 10^{-8} M).

2.3. Construction of the compact cell and potentiometric measurements:

2.3.1. Membrane preparation:

The different types of compact-cell sensor membranes were prepared as follows: 2 mg KTFPB for type-I, [1.3 mg KTFPB + 1.2 mg DZCE] for type-IIa, [1 mg KTFPB + 2 mg DZCE] for type-IIb,

and [2 mg KTFPB + 1.15 mg DZCE] for type-IIc (Table 1). The mentioned ionophore was mixed with 60–75 mg DDP plasticizers and 30–31.5 mg PVC. Then, THF was used to dissolve the mentioned components and the resulting solution was poured into 24 millimeters diameter glass ring rested on a glass plate. Finally, the obtained solution was left to dry for 24 hours at room temperature. Circles of the obtained membrane with seven millimeters diameter were cut out using a cork borer as described in an earlier report [16].

2.3.2. Cell preparation and potential measurements:

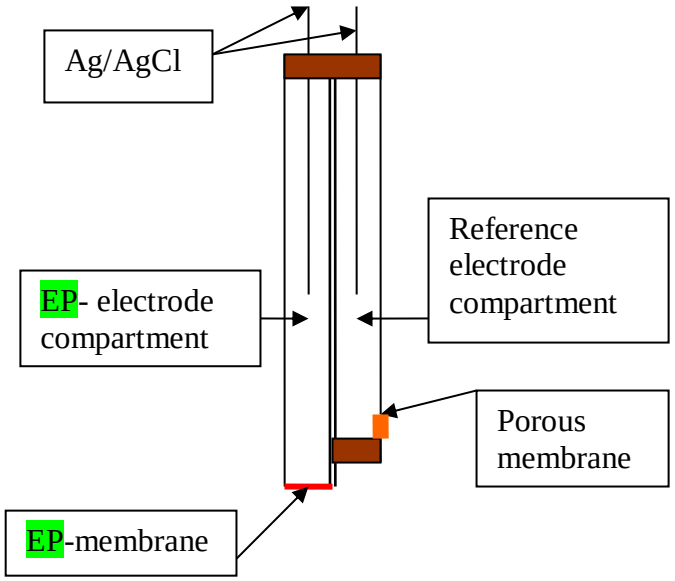


Figure 2. Schematic representation of ephedrine compact cell EP-CC.

The compact-cell was assembled using a Teflon rod (length = 10 cm, diameter = 12 mm) and was made of two separate compartments. The first compartment was the responding part of EP-CC, while the second compartment was the reference Ag/AgCl electrode. Figure 2 shows the schematic representation of the ephedrine compact-cell (EP-CC). The obtained membrane discs were fixed to the end of the EP-compartment of an EP-CC through PVC-tube. The electrode-compartment was filled with an inner aqueous filling solution (0.01 M EP and KCl). The reference compartment was filled with a 1% KCl solution.

The potential was measured at room temperature by immersing the proposed EP-CC into 50 mL water. Different aliquots of 10^{-2} and 10^{-1} M of EP were transferred to 50 mL water to make a concentration range of 10^{-8} to 9.09×10^{-3} M EP. The obtained data were recorded and graphically represented. The electrochemical EP-CC for the potential measurement can be represented as:

Ag-AgCl/1%KCl/Sample// membrane// Inner filling solution/ Ag-AgCl

where 1% KCl solution was filled in the inner compartment of the reference electrode.

The potential values were recorded and plotted against p[EP]. To monitor the influence of pH on the emf of EP-CC, NaOH or HCl (0.1 M) was used for the pH-adjustments. The emf values for EP- CC were recorded at different values of pH for 6.7×10^{-5}, 7.0×10^{-4} and 9.09×10^{-3} M EP solutions.

2.4. Calibration of EP-CC Sensor

The calculated amounts of 10^{-2} or 10^{-1} M of standard EP solution were added to 50 mL of bi-distilled water to obtain a concentration range of 10^{-8} to 9.09×10^{-3} M. The proposed EP-CC sensor was then immersed into the EP-solution. The solutions were stirred and the potentials were recorded and plotted as a function of EP-concentration. The obtained graphs were used for the subsequent determination unknown concentrations of EP.

2.5. Stability and response time of EP-CC sensor

The stability of the EP-CC was examined by monitoring the slope of the calibration curve at different time intervals (1 day, 3 days, 7 days, and 1 month). The potential reading was recorded after stabilization (±1 mV) and then, the emf was plotted as a function of the logarithm of EP concentrations. The calibration graph was constructed after the mentioned periods of time. The procedure was continued until the electrode lost its Nernstian slope.

The dynamic response of the EP-CC sensor was monitored by measuring the time required to reach a steady state potential within ±1 mV of the final equilibrium potential [20] after immersion of the sensor in 50 mL bi-distilled water. Then, the calculated amounts of EP solution were added to cover a range of 10^{-6} to 10^{-2} M.

2.6. Determination of the selectivity coefficient of EP-CC sensor

The selectivity coefficient for several cations (Na^+, K^+, Li^+, NH_4^+, Ca^{++}, Mg^{++}, and Ba^{++}), amino acids (glycine, arginine, and sodium glutamate) and pharmaceutical amines (quinine sulfate, diphenhydramine, dopamine, caffeine, and pilocarpine hydrochloride) was determined by using SSM [17,18], (see Table 2). The emf of the interference solution (0.01 M) and that for the same concentration of EP solution was measured. Then, the selectivity coefficients of EP-CC ($K_{i,j}^{pot}$) were calculated by rearranging the Nikolsky equation:

$$log\ K^{pot}_{EP^+,J^{z-}} = [(E_J\text{-}E_{EP})/S] + log\ [EP^+] - log[J^{Z-}]^{1/Z}$$

where

E_{EP}: the measured potential in 10^{-2} M ephedrine solution

E_J: the measured potential in 10^{-2} M solution of the interfering cations

S: slope of the electrode calibration plot.

2.7. Determination of ephedrine in pharmaceutical products by using the EP-CC sensor

In this procedure, 8 mg/mL of EP-sulfate injection (USP, 50 mg/mL) either from Akorn, (Akorn, Inc., Lake Forest, IL, USA); or Nexus Pharmaceuticals (Lincolnshire, IL, United States) was prepared by diluting with bi-distilled water. Alternatively, 2.5 mg from the content of an EP capsule, USP (25 mg, West-ward Pharmaceutical Corp, Eatontown, N.J., USA) was dissolved in one hundred milliliters of an aqueous solution. Afterward, 25 mL of each of the mentioned solutions was transferred to the potentiometric cell. The EP-CC sensor was immersed in 25 mL of the mentioned solutions. The potential of the solution was directly measured and compared with the calibration graph previously prepared.

3. RESULTS AND DISCUSSION

3.1. Optimization of the Membrane Composition

The performance of an EP-CC mainly depends on the membrane components [18]. The main components of the prepared membrane were a PVC-matrix, plasticizer, and ionophore as the sensing material. Each membrane component plays a specific role in the membrane function and electrode response. The incorporation of the main components of the membrane is shown in the following illustration (Figure 3):

Figure 3. Representation of incorporation of EP-membrane components together.

The ionophore compounds DZCE and KTFPB were used as an electroactive material in the construction of this new EP-CC sensor. DZCE was applied as a neutral ionophore, while the KTFPB was used a charged site for preparing the EP-CC membrane and the DDP was applied as a plasticizer in the PVC matrix. The performance characteristics of the proposed EP-CC sensor were evaluated according to the IUPAC recommendations [17]. The lower detection limit of the sensor was taken at the point of intersection of the extrapolated linear segments of the EP- calibration curve.

Table 1 shows the different parameters of the membrane compositions. Membranes type I and IIa–IIc showed the calibration graph slopes of 41.9 and 59.8–57.8, respectively. Among the tested EP-CC sensor, it was found that the cell with membrane IIa showed the best performance slope (59.8 mV/decade), the best LOD (6.3×10^{-7} M) and the widest (LR) linear range (2×10^{-6} to 9.1×10^{-3} M) (Figure 4).

Table 1. Optimization of the composition of membranes I and II used for preparing EP-CC sensor.

Name	PVC, mg	Neutral carrier, mg	(KTFPB), mg	DDP, mg	Slope, mV/Decade	R^2	LR, pM	LOD, pM
I	30	0	1	60	41.9	0.992	2.2-5.7	6.0
IIa	31.2	DZCE 1.2	1.3	75	59.8	0.9935	2.2-5.7	6.2
IIb	31.5	DZCE 2	1	67	57.8	0.9945	2.2-5.7	6.0
IIc	30.5	DZCE 1.15	2	67	57.8	0.9945	2.2-5.7	6.0

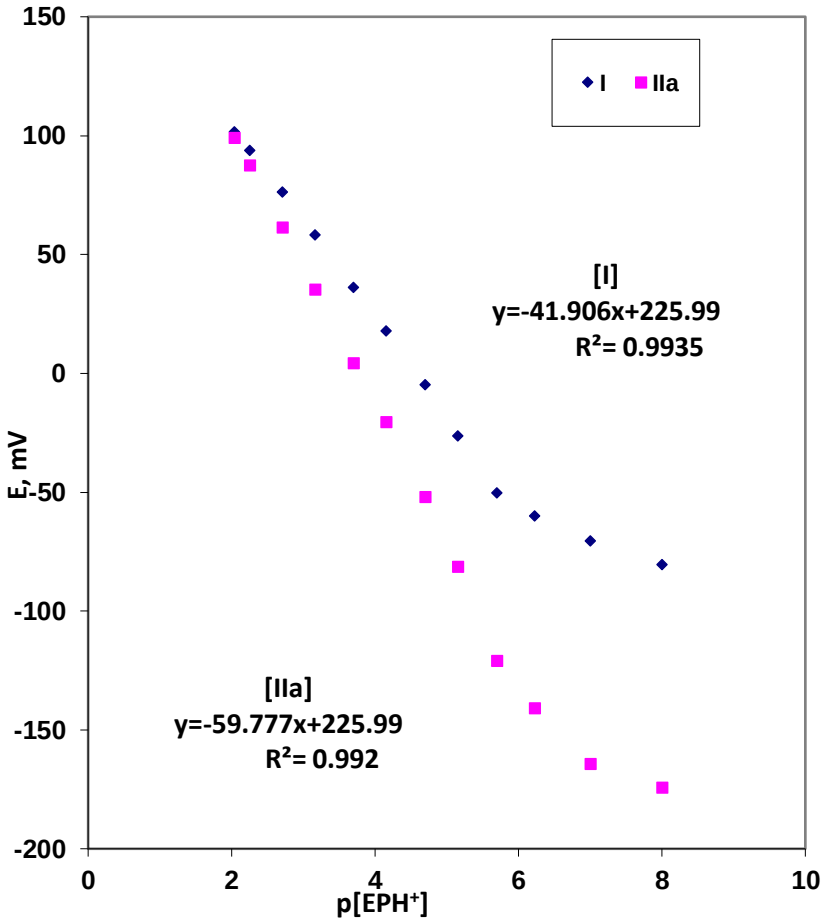


Figure 4. Calibration graph for EP-CC sensors using membranes containing either KTFPB (I) or DZCE (IIa).

From the obtained results, it was concluded that the presence of DZCE had a significant effect on the electrode slope and detection limit but had no effect on the linear range.

The response mechanism of EP-CC comprising only KTFPB can be represented as:

$$EP^+ + TFPB^- === (EP^+ - TFPB^-)$$

$$K_{eq} = [EP^{+} - TFPB^{-}] / ([TFPB^{-}] [EP^{+}])$$

In case of type-II (contains DZCE and KTFPB), the following equilibrium is expected:

$$DZCE + EP^{+} === DZCE\text{-}EP^{+}$$

$$DZCE\text{-}EP^{+} + TFPB^{-} === DZCE\text{-}EP^{+}\ TFPB^{-}$$

$$K_{eq} = [DZCE\text{-}EP^{+}\ TFPB^{-}] / ([DZCE\text{-}EP^{+}] [TFPB^{-}])$$

From the above equilibrium equations, it can be observed that in the case of sensor membrane type-I, there was an equilibrium between EP^{+} and $TFPB^{-}$. However, in the case of sensor membrane type-II, the response was based on the hosting properties of the DZCE for ephedrine cation. It was concluded that the two-step (type-II) association was more favored than the one-step association (type-I). This is because the hosting DZCE-molecule facilitated the extraction of EP-cation at the membrane site. The incorporation of membrane components (DZCE and KTFPB) for EP-CC together is illustrated in Figure 3. The typical slope value (59.8 mV/decade), the better LOD (6.3×10^{-7} M), and the wide linear range (9.1×10^{-3} to 1.99×10^{-6} M) confirmed an improvement in the EP-CC response of sensor type-II.

3.2. Stability and response time of EP-CC sensor

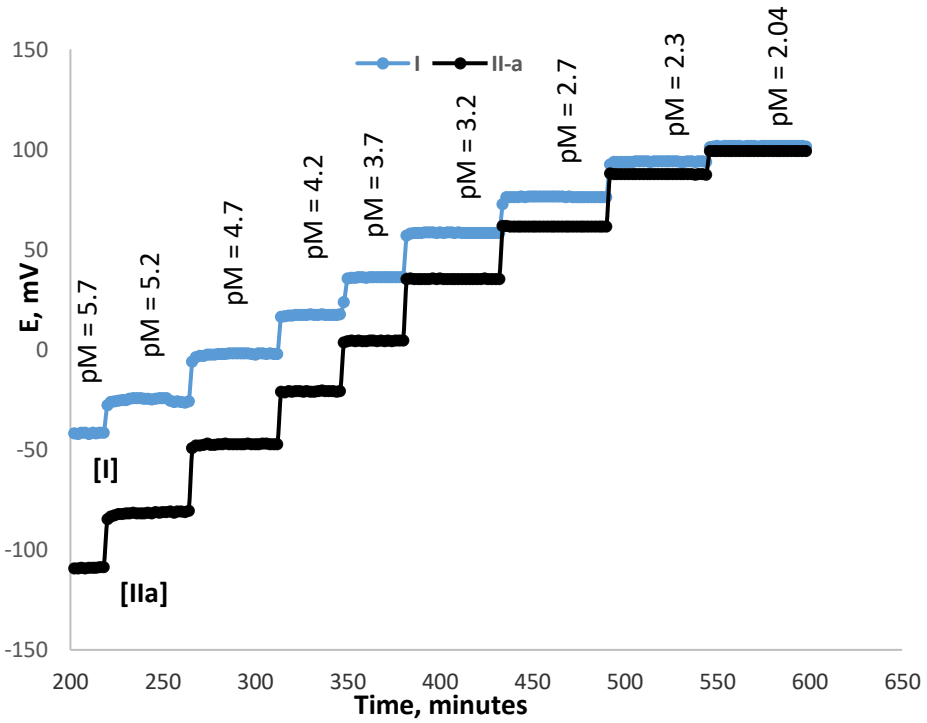


Figure 5. Potential-time curves of the proposed EP-CC using membranes containing either TFPB (I) or DZCE (IIa).

The dynamic response time is defined as the required time for the sensor to achieve the potential values within ±1 mV of the final equilibrium potential [17]. In this work, the dynamic response time of the sensor was calculated by varying the EP concentrations from 1.99×10^{-6} M to 9.1×10^{-3} M and the

response of EP-CC depended on the concentration of the EP-solutions (Figure 5). Further, it can be noticed from the figure that, for EP-CC with membrane type-IIa, the response time of the solutions of pM 3.7–2.04 was faster (4–2 s) than that for lower EP-concentrations. For the lower concentrations (pM = 5.2–4.7) the response time was (8 s). Alternatively, a longer dynamic time was observed at the same concentrations when EP-CC with membrane type-I was applied.

The stability of EP-CC was tested by recording the performance of the sensor after different time intervals (1,3,7,30 days). From the results in table 2, it can be reported that the sensor could be performed safely for one month. The only observed change was in its linear range, where the lower limit was shifted to higher value after one month (5.9×10^{-6}).

Table 2. The performance characteristics EP-CC at different time intervals.

Soaking Time, day	Slope, mV/decade	LR, M	LOD, M	R^2
1	59.8	9.1×10^{-3}- 2×10^{-6}	6.3×10^{-7}	0.9992
3	57.8	9.1×10^{-3}- 1×10^{-6}	7.9×10^{-7}	0.9945
7	56.1	9.1×10^{-3}- 2×10^{-6}	7.9×10^{-7}	0.9991
30	56.9	9.1×10^{-3}- 5.9×10^{-6}	7.9×10^{-7}	0.9997

3.3. Effect of pH:

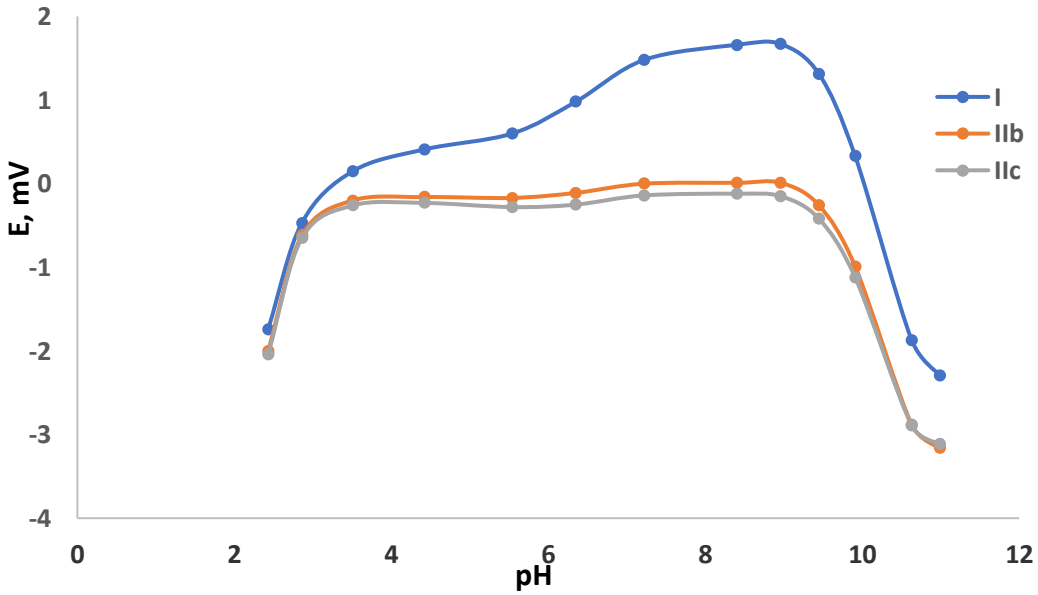


Figure 6. The relation between the solution pH and potential values of EP-CC sensor based on 1mg TFPB (I), 2mg DZCE (IIb) and 1.15 mg DZCE(IIc) when measuring 7×10^{-5} M EP-solution.

It is essential to determine the working pH-range of a sensor. Acidity affects the state of the ion-association and deteriorates some membrane components [17]. In order to study the effect of pH on the

performance of the proposed EP-CC sensor, the potential values were determined at three EP-concentrations 6.7×10^{-5}, 7.0×10^{-4} and 9.09×10^{-3} M at different pH-values. Figure 6 shows that the potential did not change in the pH range of 3.51–8.96 for EP-CC with type-II membrane. Therefore, the mentioned range was considered as an optimum pH for the EP-CC. At pH < 3.51, the EP worked like a base and accepted H^+ forming the conjugate acid. On the other hand, the potential values dropped abruptly at pH >8.96. This was expected due to the excess concentration of [OH^-]. When EP-CC with type-I membrane was used an increase in the potential was observed with an increasing pH. This is due to the sensitivity of KTFPB toward pH-changes.

3.4. Selectivity of the EP-CC

The potentiometric selectivity coefficient ($\mathbf{K^{pot}_{EP^+,J^{z+}}}$) of EP-CC was evaluated at 9.09×10^{-3} M concentration of EP for both sensor membrane types by the SSM [17-18]. The obtained data (Table 3) revealed that both of EP-CC, types-I and II, had a good selectivity for EPH^+ ions as compared to the selected cationic species either inorganic or organic and pharmaceutical amines. No interference was caused by pharmaceutical ingredients and diluents.

The obtained selectivity coefficient ($\mathbf{K^{pot}_{EP^+,J^{z+}}}$)-values of the tested compounds exhibited good selectivity toward EPH^+. For both type-I and IIa EP-CC sensor membranes, the monovalent cations (Na^+, K^+, and NH^+_4) showed $\mathbf{K^{pot}_{EP^+,J^{z+}}}$-values of an order of 10^{-2}, while Li^+ cation showed smaller value of order of 10^{-4}. The divalent cations (Ca^{++} and Mg^{++}) showed better selectivity values than monovalent cations for both EP-CC types-I and II. Ba^{++} cation showed the best value (10^{-5}) among all tested cations for both types of the EP-CC sensor membrane. The tested amino acids and pharmaceutical compounds showed suitable values of the selectivity coefficient (in order of 10^{-2}) for both types of EP-CC.

Table 3. The selectivity coefficient $\mathbf{K^{pot}_{EP^+,J^{z+}}}$-values for the proposed EP-CC type-I and type-IIa comprising either KTFPB or (KTFPB+DZCE).

Interferent	$\mathbf{K^{pot}_{EP^+,J^{z+}}}$	
	I	**IIa**
$NaNO_3$	1.5×10^{-2}	1.7×10^{-2}
KCl	1.8×10^{-2}	2.0×10^{-2}
$LiNO_3$	2.7×10^{-4}	2.8×10^{-4}
NH_4NO_3	1.6×10^{-2}	1.7×10^{-2}
$CaCl_2$	1.2×10^{-3}	1.4×10^{-2}
$Mg(NO_3)_2$	1.2×10^{-3}	1.3×10^{-2}
$Ba(NO_3)_2$	3.6×10^{-5}	6.5×10^{-5}
Glycine	1.4×10^{-2}	1.5×10^{-2}
Arginine	1.4×10^{-2}	1.6×10^{-2}
Sod Glutamate	1.6×10^{-2}	1.7×10^{-2}
Caffeine	1.0×10^{-2}	1.1×10^{-2}
Pilocarpine	2.8×10^{-2}	3.2×10^{-2}
Quinine	5.2×10^{-2}	5.8×10^{-2}
Diphenhydramine	6.0×10^{-2}	6.6×10^{-2}
Dopamine	7.1×10^{-2}	4.0×10^{-2}

3.5. Comparison of EP-CC with previous sensors

To find the advantage of the cited sensor, it is important to compare the properties of the present EP-CC sensor with the previously prepared sensors. From table 4, it is found that some of the recorded sensors [10 and 11] suffered from either strong basic working pH value (10.5). In this medium, the ephedrine base should be precipitated. The second type of sensors [16] had a working pH value in a strong acidic medium only at pH 3.2, which is a restriction for many samples. Other sensors, like [19,13, 20 and 21] had several interferences. The present EP-CC sensor did not have the restriction of pH (working pH 3.1-8.98) nor the interferences. It exhibited a value of LOD (6.3×10^{-7}), which is comparable to that of the nanocomposite sensor [10] and the amperometric sensor [11]. In addition, EP-CC sensor was designed as one set device with no need for external reference electrode like others. Also, the method did not require the preparation of ion-pair sensitive matter like most of the mentioned methods. Table 4, showed the characteristics of the present EP-CC sensor compared to the previously recorded sensors.

Table 4. Comparison between performance characteristics of different Ephedrine electrodes with the proposed EP-CC sensor.

No.	Sensitive martial	Slope (mV/ decade)	pH	Linear range (LR), M	LOD, (M)	Response time, s	Disadvantage	Ref.
1	Fe_3O_4@SiO_2@TiO_2-molecular imprinted polymer.	-	pH=10.5	9×10^{-9} - 2.8×10^{-6}	3.6×10^{-9}	-	pH 10.5 is a value where the free base precipitates.	10
2	Amperometric detection at a Co-phthalocyanine CPE.	-	In alkaline solution 0.1M NaOH	10^{-6}-10^{-4}	8.0×10^{-7}	0.320 s	In alkaline solution 0.1M NaOH. The free base precipitates.	11
3	Pt- electrode modified with poly-aminonaphthalene.	0.00096	The EP-peak appeared at 0.120 V in pH 3.2	-	0.0159	-	Measurinrg EP only at pH 3.2	16
4	PVC membrane based on phenylephrine-tetraphenylborate.	55	2.0-8.0	2×10^{-6}-10^{-1}	-	-	Interference from: Sucrose, adenine, butylamine, lucine, ornithine, tryptophan, cysteine, promethazine	13
5	EP-reineckate in PVC	56	4.0-9.0	2×10^{-6} -10^{-1}	1.6×10^{-6}	3 sec.	Interference from Quinine, phenylephrine, pyridoxine, tryptophan	19
7	EP-5-nitro-barbiturate	55.8	4.0-10.0	5×10^{-5} -10^{-2}	10^{-5}	1-10 min	Interference from: Dextromethorphan bromohidrate, caffeine	20
8	EP-TpClPB	57.5	2.5-9	2×10^{-5} -10^{-1}	4×10^{-6}	6-20 sec	Interference from: Atropine, quinidine, pilocarpine, strychnine.	21
9	Compact-cell sensor	59.8 mV/ decade	3.1–8.96	1.99×10^{-6} - 10^{-2}	6.3×10^{-7}	2-8 s	No serious interference of the tested ions.	Present work

3.6. Determination of Ephedrine in pharmaceutical products

Different EP products, ephedrine sulfate, NEXUS, and EPH 40 were assessed by the proposed EP-CC sensor. Each drug was applied by a direct potentiometric method. The measured values were in the range of 8.099–25 mg/sample and the range of recovery was between 97.8% and 98.9%. The results of the EP determination in the selected pharmaceutical samples are shown in Table 5. The determined values of EP were in a satisfactory range of the expected values. The same samples were subjected to analysis by using a previous spectrophotometric method [7]. The observed results showed that there was an agreement between both methods. The recovery range of the spectrophotometric method was (97.5-99.77%), which was close to that of the present EP-CC sensor method.

Table 5. Potentiometric assessment of ephedrine in its formulations.

Pharmaceutical preparations	**Label**	**mg/ml-taken**	**Ref. [7] mg/ml**	**Present EP-CC method mg/ml**	**RSD*, EP-CC present method**
Ephedrine sulfate injection, USP, (Akorn)	50 mg/ml	8.099	7.90	7.88	2.3
Ephedrine sulfate injection, USP, (NEXUS)	50 mg/ml	8.099	8.08	8.00	3.1
Ephedrine sulfate, capsules, USP (West-ward pharmaceutical Corp.)	25 mg/capsule	2.5	2.45	2.42	2.5

*(4-determinations)

4. CONCLUSIONS

The introduced EP-CC sensor represents a new generation of electrochemical sensors. It facilitates the assessment of EP in different samples without the need of highly expensive equipment and chemicals. The proposed cell can be introduced into online continuous monitoring system for EP in a manufacturing unit for quality control or during medical treatment. The analytical results demonstrated the requirement of sensitivity of the cell for the analysis of real samples.

ACKNOWLEDGEMENT
The authors acknowledge the financial support for this work, from the Deanship of Scientific Research (DSR), University of Tabuk, Tabuk, Saudi Arabia, under grant no. S-1439-0176.

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