Anal. Bioanal. Electrochem., Vol. 8, No. 2, 2016, 207-218

Analytical & Bioanalytical Electrochemistry

2016 by CEE
www.abechem.com

Full Paper

Comparative Study of Four Ion Selective Membrane Electrodes for Potentiometric Determination of Ivabradine Hydrochloride in Pharmaceutical Formulations and Plasma

Nadia M. Mostafa, Yasmin M. Fayez, Joliana F. Farid* and Abd El-Aziz B. Abd El-Alim

Analytical Chemistry Department, Faculty of Pharmacy, Cairo University, Kasr-El-Aini 11562-Cairo, Egypt

*Corresponding Author, Tel.: +20 1226063566

E-Mail: Joliana.farid@ pharma.cu.edu.eg

Received: 18 November 2015 / Accepted: 15 March 2016 / Published online: 31 March 2016

Abstract- Four different polyvinyl chloride (PVC) membrane sensors were investigated for the determination of ivabradine HCl in pure drug substance, pharmaceutical formulations and plasma. These sensors were fabricated using sodium tetraphenyl borate (TPB) [sensor 1a,1b,1c] or ammonium reineckate (RNC) [sensor 2a,2b] or sodium phosphotungestate (PTA) [sensor 3a,3b] or tetrakis(4-chlorophenyl)borate (TpClPB) [sensor 4a,4b] as ion exchanger. The proposed sensors showed fast and stable nernstian response range from 55.1-59.8 mV/decade across a concentration range 10^{-5}-10^{-2} M in pH range 4.5-7.5. These electrodes exhibit good selectivity for ivabradine HCl with respect to a large number of inorganic, organic cations, sugars and amino acids. The results were statistically compared with a reported method. The comparison showed no significant difference between the proposed methods and the reported method regarding both accuracy and precision.

Keywords- Ivabradine, Sodium tetraphenyl borate, Ammonium reineckate, Sodium phosphotungestate, Tetrakis(4-chlorophenyl)borate

1. INTRODUCTION

Ivabradine hydrochloride (Iva), 3-(3-{[((7S)-3,4-Dimethoxybicyclo[4,2,0]octa-1,3,5-trien-7-yl) methyl] methylamino}propyl)-1,3,4,5-tetrahydro-7,8-dimethoxy-2H-3-benzazepin-2-one,hydrochloride (Fig. 1) is a heart rate reducing agent [1]. So it is used for symptomatic management of stable angina pectoris. Ivabradine hydrochloride is a specific heart rate lowering agent, acting by reducing the rate of cardiac pacemaker activity in the sinoatrial node [2].

The literature survey reveals several methods for determination of Iva in biological fluids, in pharmaceutical dosage forms, in combination with other drugs including high performance liquid chromatography [3-19], spectrophotometric methods [6,15], Thin layer chromatography [20-23].

The development and application of ion-selective electrodes continue to be of interest for pharmaceutical analysis because these sensors offer the advantages of simple design and operation, reasonable selectivity, fast response, low cost, wide pH working range, broad concentration range and applicability to turbid and colored solutions [24].

Due to the lack of any potentiometric techniques for the determination of Iva in pharmaceutical formulations and plasma, this study was developed to validate a potentiometric method for Iva determination using four proposed sensors.

In the present work, four ion selective membrane sensors were fabricated using sodium tetraphenyl borate (TPB), ammonium reineckate (RNC), sodium phosphotungestate (PTA) and tetrakis(4-chlorophenyl)borate (TpClPB). These sensors were used for determination of Iva in pure drug substance, pharmaceutical formulations (without interference of excipients) and in plasma (without the need of preliminary extraction and separation steps).

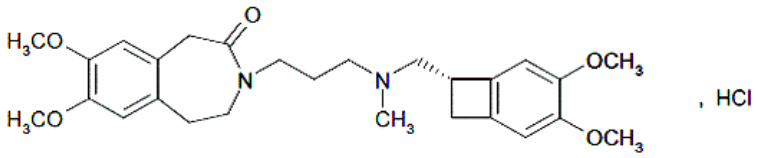

Fig. 1. Chemical structure of ivabradine hydrochloride

2. EXPERIMENTAL

2.1. Apparatus

- Jenway digital ion analyser (model 3330, UK) with Ag/AgCl double-junction type external reference electrode (No. 924017-LO-Q11C, Germany) was used.
- Jenway pH glass electrode (No. 924005-BO3-Q11C, UK) was used for pH adjustments.

2.2. Samples and pharmaceutical formulations

- Pure Ivabradine was kindly supplied by Global Napi pharmaceuticals, its purity is certified to be 100.12% according to a reported method [7].
- Procoralan® tablets, Batch No. 919844 and 947159 labeled to contain 7.5 mg/tab and 5 mg/tab respectively, manufactured by Servier (Cairo, Egypt) were purchased from local market.

2.3. Chemicals and reagents

All chemicals and reagents used throughout this work were of analytical grade and bi-distilled water was used.

- Sodium tetraphenyl borate (TPB), ammonium Reineckate (RNC), potassium tetrakis(4-chlorophenyl)borate (TpClPB) and Tetrahydrofuran (THF) were obtained from Sigma Aldrich.
- Poly (vinyl chloride) (PVC), dioctyl phthalate (DOP) and dibutyl sebacate (DBS) were obtained from Aldrich.
- 2-nitrophenyl octyl ether (NPOE) and sodium phosphotungestate (PTA) were obtained from Fluka.
- Plasma was supplied by VACSERA (Giza, Egypt)
- Phosphate buffer (pH 6) was prepared by dissolving 6.8 g of sodium dihydrogen orthophosphate in sufficient water to produce 1000 ml and adjust the pH with 10 M sodium hydroxide [25].

2.4. Stock standard solutions

- Standard stock solution of Iva (10^{-2} M) in phosphate buffer (pH 6).
- Working standard solutions of Iva (10^{-6}-10^{-3} M) were prepared by suitable dilution from its stock solution using phosphate buffer (pH 6).

2.5. Procedures

2.5.1. Fabrication of membrane sensors

2.5.1.1. Preparation of Iva-TPB membrane sensors (sensors 1a,1b,1c)

For the preparation of sensor 1a, a portion (0.19 g) of PVC was thoroughly mixed with 0.4 mL of NPOE and 0.01 g of TPB in a glass Petri dish (5-cm). The mixture was dissolved in 6 mL THF. For sensor 1b, 1c the same procedure described was followed using DBS and DOP respectively instead of NPOE.

The Petri dishes were covered with a filter paper and left to stand overnight at room temperature to allow solvent evaporation. Master membranes with thickness (0.1 mm) were

obtained and used for the construction of the electrode. From each master membrane, a disk (approximately 8 mm in diameter) was cut using a cork borer and pasted using THF to an interchangeable PVC tip that was clipped into the end of an electrode glass body. The electrodes were then filled with an internal solution of equal volumes of 10^{-3} M Iva and 10^{-3} M KCl. Ag/AgCl wire (1 mm diameter) was used as an internal reference electrode. The cell, Ag-AgCl/internal solution, 10^{-3} M Iva, 10^{-3} M KCl/PVC membrane sensor/test solution/Ag-AgCl, KCl (saturated) was assembled for measuring the emf. The electrodes were conditioned by soaking in 10^{-3} M aqueous Iva solution for 24 h and they were stored in the same solution when not in use.

2.5.1.2. Preparation of Iva- RNC membrane sensors (sensors 2a,2b)

For the preparation of sensor 2a, a portion (0.19 g) of PVC was thoroughly mixed with 0.35 mL of DOP and 0.01 g of RNC in a glass Petri dish (5-cm). The mixture was dissolved in 6 mL THF. For sensor 2b the same procedure described was followed using DBS instead of DOP. Procedure was completed as under Section 2.5.1.1 starting from “The Petri dish was covered with a filter paper and left to stand overnight . . .”.

2.5.1.3. Preparation of Iva- PTA membrane sensors (sensors 3a,3b)

For the preparation of sensor 3a, a portion (0.19 g) of PVC was thoroughly mixed with 0.35 mL of DOP and 0.01 g of PTA in a glass Petri dish (5-cm). The mixture was dissolved in 6 mL THF. For sensor 3b the same procedure described was followed using DBS instead of DOP. Procedure was completed as under Section 2.5.1.1 starting from “The Petri dish was covered with a filter paper and left to stand overnight . . .”.

2.5.1.4. Preparation of Iva-TpClPB membrane sensors (sensors 4a,4b)

For the preparation of sensor 4a, a portion (0.19 g) of PVC was thoroughly mixed with 0.35 mL of DOP and 0.01 g of TpClPB in a glass Petri dish (5-cm). The mixture was dissolved in 6 mL THF. For sensor 4b the same procedure described was followed using DBS instead of DOP. Procedure was completed as under Section 2.5.1.1 starting from “The Petri dish was covered with a filter paper and left to stand overnight . . .”.

2.5.2. Sensors calibration

The conditioned sensors were calibrated by separately transferring 50-mL aliquots of solutions (10^{-6}–10^{-2} M) of Iva into a series of 100-mL beakers. The membrane sensors, in conjunction with the Ag/AgCl reference electrode, were immersed in the above test solutions and allowed to equilibrate under stirring. The potential difference (emf) between the

membrane sensor (indicator electrode) and the reference electrode was recorded after stabilising to ±1 mV, and the emf was plotted as a function of the logarithm of Iva concentration. The regression equations for the linear part of the curves were computed and used for subsequent determination of unknown concentrations of Iva.

2.5.3. Sensors selectivity

A number of pharmaceutical additives and diluents commonly used in drug formulations were examined for their effect on the assay method. Potentiometry selectivity coefficients ($K^{pot}_{A,B}$) were evaluated according to IUPAC guidelines using the separate solutions method [26] in which the potential of cell compromising the membrane electrode and a reference electrode is measured with two separate solutions, A and B where A (Drug ions) and B (interfering ion) at the same activity $a_A=a_B$.

Different interfering cations at a concentration of 10^{-3} M at a suitable pH were utilized and the results were obtained using the following equation

$$Log\ K^{pot}_{A,B} = \frac{E_B - E_A}{S} + \left(1 - \frac{Z_A}{Z_B}\right) \log a_A \quad (1)$$

Where E_A and E_B are the measured potential reading recorded after exposing the electrode to the same concentration of the studied drug and interfering ion respectively. ($K^{pot}_{A,B}$) is the potentiometric selectivity coefficient, S the slope of the calibration plot (mV/concentration decade), a_A the activity of drug and Z_A and Z_B are the charges on drug and the interfering ion, respectively.

2.5.4. Application to pharmaceutical formulations

Ten tablets of Procoralan® tablets were weighed and powdered. An accurate weight of the powdered tablets was transferred to a 50 mL volumetric flask and the volume was completed to the mark with phosphate buffer (pH 6) to prepare a 10^{-3} M solution of Iva. The emf produced by immersing the prepared sensors in conjunction with double junction Ag/AgCl reference electrode in the prepared solutions was determined then the concentration of Iva was calculated from the regression equation of the corresponding electrode.

2.5.5. Application to plasma sample

4.5 ml of human plasma were placed into two stoppered shaking tubes, then 0.5 ml of 10^{-2} and 10^{-3} M Iva were added separately and shacked. The prepared sensors were immersed in conjunction with the double junction Ag/AgCl reference electrode in these solutions. The membrane sensor was washed with water between measurements. The emf

produced for each solution was measured by the proposed sensors then the concentration of Iva was determined from the corresponding regression equations.

3. RESULTS AND DISCUSSION

3.1. Sensors fabrication

The development and application of ion selective electrode continue to be of interest for pharmaceutical analysis because these sensors offer the advantages of simple design, reasonable selectivity and fast response. The advantages of the suggested potentiometric sensors are their low cost, wide pH working range, wide concentration range and applicability to turbid and colored solutions. The present investigation is based on the fact that Iva behaves as a cation. This property suggests the use of cationic type of ion exchanger, sodium tetraphenyl borate, ammonium reineckate, sodium phosphotungestate and tetrakis (4-chlorophenyl)borate with low solubility product and suitable grain size. They are physically compatible with the matrix and play the role of rapid ion exchanger for Iva at the membrane-sample interface.

PVC acts as standard support matrix and as traps for the sensed ions. It has the advantages of chemical inertness, high tensile strength and low cost, but its use makes a need for a plasticizer.

3.2. Sensors calibration and response time

DOP shows higher Nernstian slope when used with (RNC, PTA, TpClPB) than that of DBS while DBS shows faster response and lower values of intercept with (RNC, PTA). NPOE is found to be the best plasticizer used with TPB showing better Nernstian slope than that of DOP and DBS.

Electrochemical performance characteristics of the proposed sensors were evaluated according to the IUPAC recommendation data [26], Table 1. Typical calibration plots are shown in Fig. 2 – 5. It was found that the electrodes displayed constant and stable potential readings within 2 mV from day to day and the calibration slopes did not change by more than 2 mV per decade over a period of 1 month. The response time of the electrode was tested for concentrations of Iva from 10^{-6}-10^{-2} M. The measurements were characterized by a fast stable response within 15–20 s for sensors 1a, 2b, 4a and 20–30 s for sensors 1b, 1c, 3b, 4b and 30–40 s for sensors 2a, 3a.

Long term potential stability of the proposed sensors was fairly good as it practically unchanged over a period of 7–9 weeks for sensors 1a,1b and 5–7 weeks for sensors 1c, 2b, 3a, 4a, 4b and 3–5 weeks for sensors 2a, 3b.

Table 1. Response characteristics of the investigated sensors.

Parameters	Sensor 1			Sensor 2		Sensor 3		Sensor 4	
	1a	1b	1c	2a	2b	3a	3b	4a	4b
Slope (mV/decade)	57.8	54.2	45.6	55.1	47.7	59.8	52	57.4	56.2
Intercept (mV)	332.3	327.8	312.1	306.8	275.2	390.3	301.3	334.1	294.7
Correlation coefficient	0.9999	0.9995	0.9991	0.9998	0.9994	0.9999	0.9998	0.9999	0.9999
Response time (s)	15 – 20	20 – 30	20 – 30	30 – 40	15 – 20	30 – 40	20 – 30	15 – 20	20 – 30
Working pH range	4.1 – 7.2	4.1 – 7.2	4.1 – 7.2	4.1 – 7.2	4.1 – 7.2	4.1 – 7.2	4.1 – 7.2	4.1 – 7.2	4.1 – 7.2
Concentration range (M)	10^{-5}-10^{-2}	10^{-5}-10^{-2}	10^{-5}-10^{-2}	10^{-5}-10^{-2}	10^{-5}-10^{-2}	10^{-5}-10^{-2}	10^{-5}-10^{-2}	10^{-5}-10^{-2}	10^{-5}-10^{-2}
Life span (weeks)	7 – 9	7 – 9	5 – 7	3 – 5	5 – 7	5 – 7	3 – 5	5 – 7	5 – 7
Average recovery (%)	99.98	99.96	100.20	100.00	99.78	99.98	99.96	99.99	99.97
R.S.D. *	0.34	0.75	1.03	0.47	0.98	0.33	0.57	0.37	0.52

* Average of five determinations

3.3. Effect of pH and temperature

For quantitative measurements with ion selective electrodes, studies were carried out to reach the optimum experimental conditions. The pH effect was studied to be optimized from the point of view of both sensor function and chemical form of the test substance. It was apparent from the potential-pH profiles, Fig. 6-9, that the sensor responses are fairly steady over pH 4.1-7.2. Within this range, the drug cations were completely ionized, dissociated and therefore they become sensible; above and below this pH range, the potentials displayed by the electrodes were noisy. The potentiometric response of the electrodes at the optimum pH was linear with constant slopes over a drug concentration range 10^{-5}-10^{-2} M for all the proposed sensors. The temperature effect was also studied. The results suggested that the proposed membrane sensors exhibit a steady response indicating thermal stability of PVC membranes up to 35 °C.

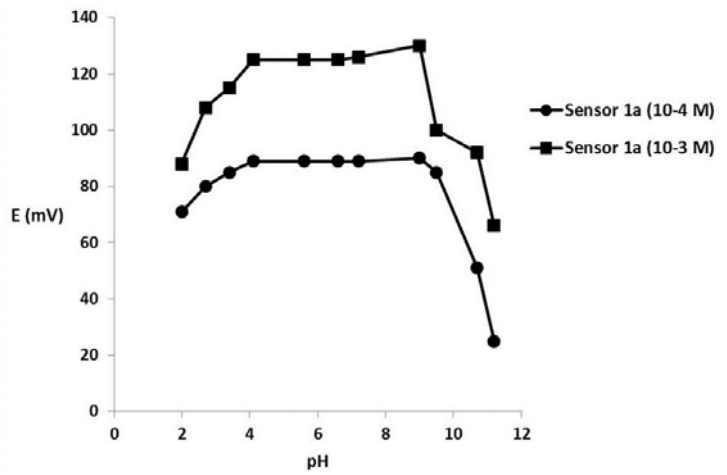

Fig. 6. Effect of pH on the response of sensor 1a

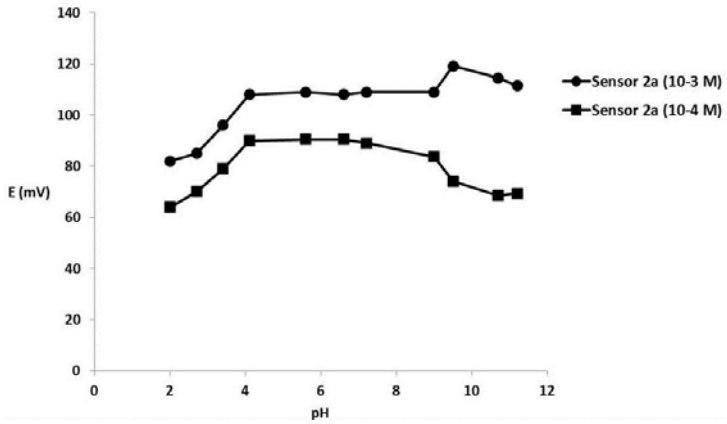

Fig. 7. Effect of pH on the response of sensor 2a

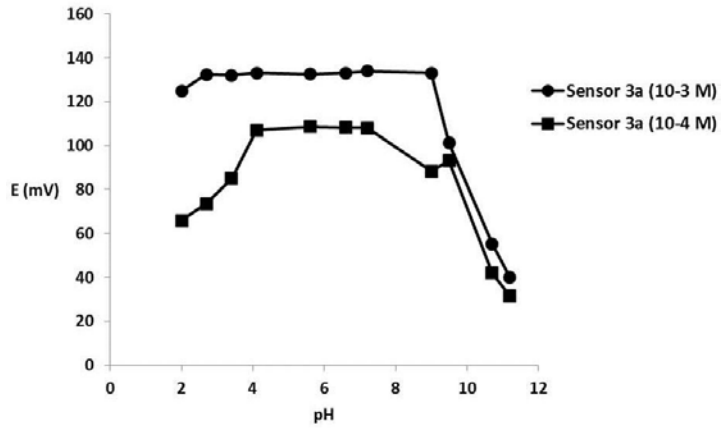

Fig. 8. Effect of pH on the response of sensor 3a

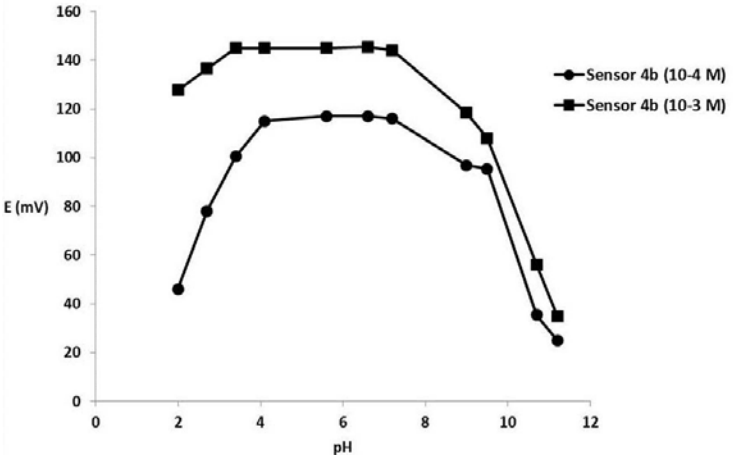

Fig. 9. Effect of pH on the response of sensor 4b

3.4. Sensors selectivity

Table 2 shows the potentiometric selectivity coefficients of the proposed sensors in the presence of tablet excipients, organic and inorganic related substances; the results revealed that the proposed membrane sensors displayed high selectivity, and that no significant interference was observed from interfering species.

Table 2. Potentiometric selectivity coefficients of the proposed electrode using separate solutions method [25]

Interferent*	Sensor 1			Sensor 2		Sensor 3		Sensor 4	
	1a	1b	1c	2a	2b	3a	3b	4a	4b
Na^+	9.5×10^{-3}	3.1×10^{-2}	10.9×10^{-3}	5.7×10^{-3}	9.3×10^{-3}	6.7×10^{-3}	1.3×10^{-2}	8.2×10^{-3}	6.4×10^{-2}
K^+	8.9×10^{-3}	3.1×10^{-2}	8.5×10^{-3}	8.9×10^{-3}	9.6×10^{-3}	7.8×10^{-3}	1.2×10^{-2}	8.2×10^{-3}	5.2×10^{-2}
NH_4^+	8.4×10^{-3}	3.0×10^{-2}	8.0×10^{-3}	9.8×10^{-3}	8.9×10^{-3}	7.1×10^{-3}	1.2×10^{-2}	8.4×10^{-3}	5.4×10^{-2}
Ca^{2+}	8.2×10^{-3}	3.2×10^{-2}	7.7×10^{-3}	11.6×10^{-3}	9.8×10^{-3}	9.1×10^{-3}	1.5×10^{-2}	7.6×10^{-3}	5.0×10^{-2}
Mg^{2+}	8.1×10^{-3}	3.3×10^{-2}	9.9×10^{-3}	10.7×10^{-3}	10.2×10^{-3}	7.0×10^{-3}	1.3×10^{-2}	7.7×10^{-3}	4.5×10^{-2}
Urea	8.7×10^{-3}	3.0×10^{-2}	7.8×10^{-3}	13.4×10^{-3}	9.6×10^{-3}	8.6×10^{-3}	1.5×10^{-2}	7.9×10^{-3}	4.6×10^{-2}
Talc	8.2×10^{-3}	3.0×10^{-2}	9.8×10^{-3}	14.3×10^{-3}	10.8×10^{-3}	8.0×10^{-3}	1.4×10^{-2}	7.2×10^{-3}	4.0×10^{-2}
Starch	8.4×10^{-3}	3.1×10^{-2}	8.5×10^{-3}	9.8×10^{-3}	8.7×10^{-3}	6.6×10^{-3}	1.3×10^{-2}	6.6×10^{-3}	4.5×10^{-2}
Sucrose	8.7×10^{-3}	3.1×10^{-2}	7.5×10^{-3}	11.8×10^{-3}	8.5×10^{-3}	6.7×10^{-3}	1.5×10^{-2}	6.1×10^{-3}	4.8×10^{-2}
Glucose	7.6×10^{-3}	2.9×10^{-2}	8.3×10^{-3}	14.6×10^{-3}	9.6×10^{-3}	6.1×10^{-3}	1.4×10^{-2}	6.5×10^{-3}	4.4×10^{-2}
Lactose	7.7×10^{-3}	3.0×10^{-2}	8.0×10^{-3}	13.7×10^{-3}	9.8×10^{-3}	6.3×10^{-3}	1.5×10^{-2}	5.5×10^{-3}	4.1×10^{-2}

* All interferents were in the form of 10^{-3} M

3.5. Application to pharmaceutical formulations

Pharmaceutical additives, diluents and ingredients commonly used in drug formulations such as lactose, sucrose, starch and talc did not show any interference. Thus, the analysis was carried out without prior treatment or extraction. The method was successfully used for the determination of Iva in Procoralan® tablets, as shown in Table 3.

Table 3. Determination of Iva in Procoralan® tablets by the proposed sensors

Pharmaceutical formulations	Recovery (%) ± S.D. *								
	Sensor 1			Sensor 2		Sensor 3		Sensor 4	
	1a	1b	1c	2a	2b	3a	3b	4a	4b
Procoralan®5mg	100.91±0.306	100.64±0.574	101.34±0.194	99.30±0.375	101.10±0.740	99.58±0.532	98.92±0.340	99.29±0.514	99.62± 0.786
Procoralan®7.5mg	100.81±0.408	99.16±0.826	100.22±0.517	99.68±0.300	101.50±0.247	100.14±0.670	99.84±0.453	99.45±0.411	100.36±0.419

* Average of five determinations

3.6. Application to plasma sample

On application to plasma, it has been found that the four electrodes gave stable results as revealed by high precision and accuracy of recoveries of the spiked human plasma samples without interference from any components in the plasma which represent the main advantage of ion selective electrode method (Table 4).

Statistical evaluation of the results of analysis of pure Iva by the proposed electrodes and the reported method [7] showed that there is no significant difference between the proposed and reported method in terms of accuracy and precision (Table 5).

Table 4. Determination of Iva in spiked human plasma by the proposed sensors

Concentration (M)	Recovery (%)±S.D. *								
	Sensor 1			Sensor 2		Sensor 3		Sensor 4	
	1a	1b	1c	2a	2b	3a	3b	4a	4b
10^{-3}	99.80±0.287	99.01±0.134	98.84±0.469	99.04±0.499	100.91±0.637	100.21±0.368	98.75±0.247	99.71±0.581	99.94±0.426
10^{-4}	99.46±0.371	100.14±0.618	99.53±0.333	98.80±0.566	100.74±0.348	98.98±0.494	99.66±0.481	98.77±0.890	98.53±0.675

* Average of three determinations

Table 5. Statistical analysis of the results obtained by the proposed sensors and the reported method for determination of Iva in pure powder form

	Sensor 1			Sensor 2		Sensor 3		Sensor 4		Reported
	1a	1b	1c	2a	2b	3a	3b	4a	4b	method [7]*
Mean	99.98	99.96	100.20	100.00	99.78	99.98	99.96	99.99	99.97	100.12
S.D.	0.343	0.750	1.030	0.467	0.982	0.332	0.565	0.365	0.524	0.463
Variance	0.118	0.563	2.519	0.218	1.309	0.110	0.319	0.133	0.118	0.2148
n	4	4	4	4	4	4	4	4	4	6
Student's t-test (2.262) **	0.553	0.384	0.141	0.403	0.643	0.561	0.474	0.499	0.468	
F value **	1.83 (9.01)	2.62 (5.41)	4.94 (5.41)	1.02 (5.41)	4.49 (5.41)	1.95 (9.01)	1.49 (5.41)	1.61 (9.01)	1.28 (5.41)	

* HPLC method using C_{18} column, methanol:25 mM phosphate buffer (60:40 v/v) as a mobile phase and UV detection at 285 nm

** Figures between parentheses represent the corresponding tabulated values of t and F at P = 0.05.

4. CONCLUSION

The described sensors are sufficiently simple and selective for the quantitative determination of Iva at a wide concentration range (10^{-5} to 10^{-2}) in pure, pharmaceutical formulations and in plasma.

The use of the proposed sensors offers the advantages of fast response, elimination of drug pretreatment or separation steps, low detection limit and direct determination of drugs in turbid and colored solutions. They can therefore be used for routine analysis of the drugs in quality control laboratories.

REFERENCES

[1] T. G. Department of health and ageing, Administration (2012).

[2] E.M. Agency., in, EMA (2005).

[3] P. Klippert, J. P. Jeanniot, S. Polvé, C. Lefèvre, and H. Merdjan, J. Chromatog. B 719 (1998) 125.

[4] M. François-Bouchard, G. Simonin, M. J. Bossant, and C. Boursier-Neyret, J. Chromatog. B 745 (2000) 261.

[5] X. Y. CUI, X. J. SHI, and Z. D. L. I. M. K. Zhong, Chinese Pharm. J. 4 (2010) 024.

[6] S. Maheshwari, A. P. Khandhar, and A. Jain, Eurasian J. Anal. Chem. 5 (2010) 53.

[7] S. Seerapu, and B. Srinivasan, Indian J. Pharm. Sci. 72 (2010) 667.

[8] X. Jin, C. T. Lu, Y. L. Feng, L. K. Ding, Y. Guan, W. Sun, L. Zhou, and A. D. Wen, Prog. Modern Biomed. 14 (2011) 004.
[9] N. Li, X. J. Shi, Z. L. Zhang, and M. K. Zhong, Chinese Pharm. J. 15 (2011) 019.
[10] Y. Y. Jia, C. T. Lu, Y. Song, L. K. Ding, J. Yang, M. C. CHEN, X. Q. Li, W. Song, L. Zhou, and Z. J. Feng, J. Chinese Mass Spect. Soc. 2 (2012) 004.
[11] C. Lu, Y. Jia, J. Yang, X. Jin, Y. Song, W. Liu, Y. Ding, X. Sun, and A. Wen, Acta Pharm. Sinica B 2 (2012) 205.
[12] Y. Na, F. Ke-zhong, and L. A-li, Qilu Pharm. Affairs 5 (2012) 012.
[13] X. Yang, Q. Zhang, and H. Li, Northwest Pharm. J. 5 (2012) 013.
[14] J. Jiang, L. Tian, Y. Huang, and Y. Li, Biomed. Chromatog. 27 (2013) 1603.
[15] S. Panda, and S. Patra, PharmaTutor 2 (2014) 201.
[16] P. Selva Kumar, K. Pandiyan, K. Rajagopal, World J. Pharm. Pharm. Sci. (2014).
[17] Y. Xiaoli, L. Hui, and L. Cui, Chinese Pharm. Affairs 5 (2011) 022.
[18] C. Roig, G. Gauto, N. Ibarrola, M. Duarte, L. Monges, D. Romero, and A. Riva, Memorias del Instituto de Investigaciones en Ciencias de la Salud 10 (2012) 63.
[19] A. A. Zoerner, C. Schroeder, A. A. Kayacelebi, M. T. Suchy, F. M. Gutzki, D. O. Stichtenoth, J. Tank, J. Jordan, and D. Tsikas, J. Chromatog. B 927 (2013) 105.
[20] M. H. Motisariya, K. G. Patel, and P. A. Shah, Bulletin of Faculty of Pharmacy, Cairo University, 51 (2013) 233.
[21] P. Pikul, J. Nowakowska, and K. Ciura, J. Food Drug Anal. 21 (2013) 165.
[22] P. Pikul, J. Nowakowska, and K. Ciura, J. Liquid Chromatog. Relat. Technol. 37 (2014) 1837.
[23] M. Damle, and R. Bagwe, Pharm. Sci. Monitor 6 (2015) 141.
[24] V. V. Coşofret, and R. P. Buck, Critical Rev. Anal. Chem. 24 (1993) 1.
[25] British Pharmacopoeia, Stationary Office, London, Appendix 1D (2007).
[26] IUPAC Analytical Chemistry Division, Commission on Analytical Nomenclature, Pure Appl. Chem. 72 (2000) 1851.