Int. J. Electrochem. Sci., 10 **(2015)** 1447 - 1458

International Journal of
ELECTROCHEMICAL
SCIENCE
www.electrochemsci.org

Clenbuterol Determination in Pharmaceutical Formulation by Potentiometric Membrane Sensor

Farnoush Faridbod[1,2,*], *Masoomeh Dorrani*[1]

[1] Center of Excellence in Electrochemistry, Faculty of Chemistry, University of Tehran, Tehran, Iran
[2] Biosensor Research Center, Endocrinology & Metabolism Molecular-Cellular Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran
[*]E-mail: faridbodf@khayam.ut.ac.ir

Received: 31 October 2014 / *Accepted:* 5 December 2014 / *Published:* 16 December 2014

Clenbuterol is a selective β_2-adrenoceptor agonist which has been known as a thermogenic drug. This work introduces design and construction of a PVC membrane sensor for fast and simple determination of Clenbuterol in pharmaceutical formulation. The designed electrochemical sensor responds based on ion-pair exchange mechanism. Clenbuterol-Tetraphenyl borate was synthesized and used as sensing element of the membrane. After a series of experiments, the best electrode performance was selected with a membrane composition of 30% PVC, 60% DBP, 2% room temperature ionic liquid and 8% ion-pair. Room temperature ionic liquid was used as an additive and improves the sensitivity of the sensor. This electrode has a rather fast (~34 s), stable and Nernstian response (57.5±0.4 mV/decade) in a wide concentration range of 5.3×10^{-6} to 1×10^{-2} mol L^{-1}, and applicable pH range of 3-6. Validation of the method shows suitability of the sensors for analysis of Clenbuterol in pharmaceutical tablets. The sensor shows good repeatability with RSD of 4.7%.

Keywords: Clenbuterol, Potentiometry, PVC membrane, Ion selective electrode, Ion-Pair complex, Ionic liquids

1. INTRODUCTION

Clenbuterol, 4-Amino–3,5–dichloro-α-[[(1,1–dimethylethyl)amino] methyl] benzenemethanol (Figure 1), is a selective β_2-adrenoceptor agonist, which has been known as a thermogenic drug, and it is widely used orally in the treatment of asthma [1]. Clenbuterol is a β_2 agonist with some structural and pharmacological similarities to epinephrine and salbutamol, but its effects are more potent and longer-lasting as a stimulant and thermogenic drug.

Due to its powerful capacity to improve growth rate and reduce carcass fat, it has also been popularly abused as a food additive for live-stocks and stimulant for athletes [2]. Clenbuterol has been a serious threat to human health. When animals are treated with β_2-agonist, residues can accumulate in their meat and liver which may have a pharmacological effect in human body [3-4] and may pose severe threat to human health, include acute poisoning with symptoms of muscular tremor, cardiac palpitation, vomiting, nausea, nervousness and chills [5]. Clenbuterol is not an ingredient of any therapeutic drug approved by US Food and Drug Administration. It is also banned for IOC-tested athletes. In the US, administration of Clenbuterol to any animal that could be used as food for human consumption is banned by the FDA. However, Clenbuterol is still a therapeutic drug for asthma in human in some countries. Also, it is used by some body builders to lose weight.

Hence, it is essential to have a fast, sensitive, and cost-effective technique to detect the presence of this organic compound. Various analytical methods for analysis of Clenbuterol have been reported, including high-performance liquid chromatography [6], gas chromatography–mass spectrometry [7,8], potentiometry using molecularly imprinted polymer sensor [9], capillary electrophoresis [10], radioimmunoassay [11] and enzyme immunoassay [12], and voltammetric methods [13,14].

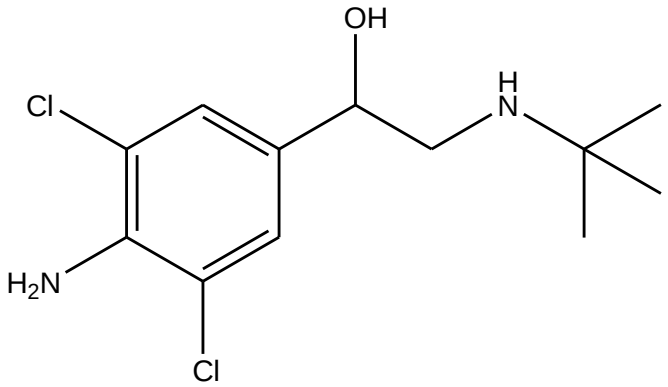

Figure 1. Chemical structure of Clenbuterol

Different electrochemical measurement techniques were used for drug analysis during recent years but potentiometric using indicator electrodes have advantages of rapid and ease of preparation and procedures, fast response time, reasonable selectivity, wide linear dynamic range, and low cost. These characteristics have certainly led to the preparation of numerous sensors for several ionic species, and the number of available electrodes has grown largely during the past years [15-19]. PVC membrane electrodes are one of the subdivisions of potentiometric sensors which are widely used and have different application in analysis of ionic species [20-33].

In this work, the proposed electrode works based on ion-pair complex. It was made from the interaction between Clenbuterol hydrochloride and sodium tetraphenyl borate and they respond according to the ion-exchange mechanism. PVC membrane electrode was made after series of experiments. Also, different room temperature ionic liquids (RTILs), 1-n-butyl-3-methylimidazolium

tetrafluoroborate ([bmim]BF_4), 1-n-butyl-3-methylimidazolium hexafluorophosphate ([bmim]PF_6), and 1-octyl-3-methylimidazolium tetrafluoroborate ([omim]BF_4) was used as additives in the composition of the liquid membrane to improve the sensitivity of the proposed sensor.

2. EXPERIMENTAL SECTION

2.1. Apparatus

A glass cell where the Clenbuterol PVC membrane sensor as an indicator electrode was placed; consisted of two Ag/AgCl double junction reference electrodes (Azar-Elelectrode Co., Iran) as internal and external reference electrodes. Both electrodes were connected to an ion analyzer with a 250 pH/mV meter with ±0.1 mV precision.

2.2. Materials and Reagents

Chemicals (of analytical reagent grade) were: high-molecular weight polyvinylchloride (PVC) (Fluka Co.), sodium tetraphenyl borate (NaTPB), dibutyl phthalate (DBP), nitrobenzene (NB), benzyl acetate (BA), *o*-nitrophenyloctylether (*o*-NPOE), and tetrahydrofuran (THF) (Merck Co.). Room temperature ionic liquids, 1-n-butyl-3-methylimidazolium tetrafluoroborate ([bmim]BF_4), 1-n-butyl-3-methylimidazolium hexafluorophosphate ([bmim]PF_6), and 1-octyl-3-methylimidazolium tetrafluoroborate ([omim]BF_4) were taken from Iran Petroleum Industry Institute. All materials were of the highest available purity without further modification. Clenbuterol hydrochloride was purchased from Sigma-Aldrich and its pharmaceutical formulations were obtained from a local pharmacy (Tehran, Iran).

2.3. Synthesis of the ion-pair complex

Sensing element used in the membrane of the sensor was an ion-pair compound which is made from the interaction of Clenbuterol hydrochloride and sodium tetraphenyl borate.

Sodium tetraphenyl borate (NaTPB) is the organic compound shown in Fig. 2. It is a salt, where in the anion consists of four phenyl rings bonded to boron. The compound is used in inorganic and organometallic chemistry as a precipitating agent. This white crystalline solid is water soluble. It can be used to form tetraphenyl borate base salts, which are often insoluble in water.

Clenbuterol is most available as the hydrochloride salt, Clenbuterol hydrochloride. It is a colourless, microcrystalline powder (M.P. 174°C to 175.5°C). It is very soluble in water, methanol and ethanol.

To synthesis the ion-pair compound, 20 mg Clenbuterol hydrochloride was dissolved in 15 mL distilled water. 20 mg sodium tetraphenyl borate was dissolved in 5 mL distilled water and then it was slowly added to the Clenbuterol solution. A white precipitate forms. The resulting precipitate was then filtered, washed with distilled water and dried in room temperature for further usage [20,25].

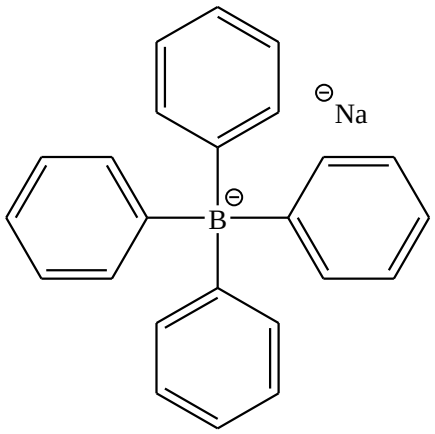

Figure 2. Chemical structure of sodium tetraphenylborate

2.4. Preparation of the liquid membrane

General procedure to prepare the membrane of the sensor was as follow: different amounts of ion-pair along with appropriate amounts of PVC, plasticizer and additive (RTIL) were dissolved in tetrahydrofuran (THF), and the solution was mixed well into a glass dish of 2 cm diameter. Then, THF was evaporated slowly until an oily concentrated mixture was obtained. A plastic tube (about 3 mm o.d.) was dipped into the mixture for about 10 s so a transparent membrane of about 0.3 mm in thickness was formed. The tube was then pulled out from the mixture and kept at room temperature for about 5 h. Afterwards, the tube was filled with an internal filling solution (1.0×10^{-3} mol L^{-1} of Clenbuterol hydrochloride solution). The electrode was at last conditioned for 15 h by soaking in the same solution [20-23].

2.5. Clenbuterol standard solutions

As mentioned above, Clenbuterol hydrochloride is soluble in aqueous solutions. A solution of 0.02 mol L^{-1} Clenbuterol hydrochloride was prepared as stock solution. The working standard solutions (1×10^{-7} to 1×10^{-2} mol L^{-1}) were then prepared by appropriately dilution of the stock solution with distilled water. The solution kept in refrigerator (4°C) when not in use.

2.6. Cell assembly for potentiometric measurement

Following cell assembly for Potentiometric measurements were used:

Ag-AgCl || internal solution, 1×10^{-3} mol L^{-1} Clenbuterol hydrochloride solution | PVC membrane | sample solution || Ag-AgCl, KC1 (satd.)

These measurements were done using calibration method with several standard solutions.

2.7. Sample preparation for the real assay

Twenty tablets of Clenbuterol hydrochloride finely powdered. Portions equivalent to the weight of 5 to 10 tablets (each tablet contain 0.04 mg Clenbuterol) were weighed and transferred into a 10-mL volumetric flask. Distilled deionized water was then added. The contents were shaken thoroughly to dissolve the compound, then made up to volume and adjust the pH to 4.5 with acetate buffer (0.1 mol L^{-1}). Suitable aliquots of this solution were filtered through a Millipore filter (0.45 mm).

3. RESULTS AND DISCUSSION

A drug selective potentiometric sensors, provides a new approach for analysis of pharmaceutics in formulations. Although sensitivity and limit of detection of these devices are not comparable with advanced instrumental methods, they can offer a fast and easy method of analysis especially for determination of compounds in formulations. One of the wide classes of potentiometric sensors are PVC membrane based sensors. The ingredients used in the membrane can have important effects on the response of the sensor.

3.1. PVC Membrane ingredients

PVC matrix, a suitable plasticizer and an ion-pair compound are the main components of a drug membrane sensor. Each one plays a special role in the sensor response. Some of the important optimizations of the membrane ingredients are shown in Table 1. As a general procedure a plasticizer/PVC ratio about 2.2 is the best amount for making the membrane [34-38]. Thus, for all the membranes presented in Table 1, 30%wt. PVC has been selected and not shown.

Besides the PVC matrix, a water-immiscible organic solvent should be used to plasticize the membrane. It helps the mobility of the ion-pair complex inside the membrane [39-41]. The plasticizer should have a low vapor-pressure, compatible with PVC, no functional groups which can undergo protonation reactions. General plasticizers with a variety of dielectric constants, dibutyl phthalate (DBP with DC of 6.4), nitrophenyloctyl ether (*o*-NPOE with DC of 24), nitrobenzene (NB with DC of 35.7) and benzylacetate (BA with DC of about 5.7) were used. DBP better showed the better responses. Since drug molecules are normally large hydrophobic species, a low polarity plasticizer extract them better in the organic phase of the membrane. Although plasticizer helps the better extraction and exchanging the drug ions, sometimes it cannot be very successful. In this case, adding small amount of ionic additive can be improve the exchange mechanism and reduce the Ohmic resistance. A new recent approach for optimization of the response of the sensor is using a water-immiscible room temperature ionic liquid in the membrane composition. RTILs can be act as an ionic additive and beside decreasing the membrane Ohmic resistance; they can also improve the ion-exchanging. As it can be seen in Table 1, three room temperature ionic liquids were used in the composition of the membrane no. 8 to no. 13. Results shows that using [bmim]PF_6 helps the Clenbuterol ions better exchange from the aqueous solution to the organic phase of the membrane.

Miscibility of RTILs with water is defined by their hydrophobic properties. ILs can be water-

immiscible or hydrophobe which mostly depends on the type of cationic and anionic bases of ILs. The miscibility of ILs in water is strongly dependent on their anions. Cl^-, Br^-, I^-, NO_3^-, CH_3COO^- and CF_3COO^- are anions that make the ILs miscible with water. ILs composed of anions such as PF_6^- and Tf_2N^- are in immiscible with water. Miscibility of anions such as BF_4^- is dependent on the structure of the cations. Although in general they are miscible with water, the miscibility will decrease with the increase in the cation chain length which is due to the increased surface activity of the longer chain cations [15,42,43]. The hydrophobe ILs are better candidates for using in making electrochemical sensors because these electrochemical devices contact with water during their operations.

Table 1. Various membrane ingredients used in making Clenbuterol PVC membrane sensor

No	Plasticizer	Ion-pair	RTIL	Slope* mV/decade	LR (mol L^{-1})*	DL (mol L^{-1})*	Response time	R^2
1	DBP,66	4	-	19.3±0.7	5.0×10^{-4}-1.0×10^{-3}	5.0×10^{-4}	1.5 min	0.789
2	DBP,64	6	-	38.6±0.5	1.0×10^{-4}-1.0×10^{-3}	9.0×10^{-5}	1 min	0.914
3	DBP,62	8	-	48.5±0.5	5.0×10^{-5}-5.0×10^{-3}	6.5×10^{-5}	50 s	0.927
4	DBP,60	10	-	44.5±0.6	5.0×10^{-5}-5.0×10^{-3}	5.0×10^{-5}	52 s	0.954
5	NB,62	8	-	17.7±0.6	1.0×10^{-4}-1.0×10^{-3}	1.0×10^{-4}	1 min	0.896
6	NPOE,62	8	-	32.6±0.5	10×10^{-4}-5.0×10^{-3}	1.0×10^{-4}	1 min	0.945
7	BA,62	8	-	36.2±0.5	1.0×10^{-4}-1.0×10^{-2}	5.0×10^{-5}	55 s	0.936
8	DBP,61	8	1[bmim]PF_6	52.7±0.5	1.0×10^{-5}-1.0×10^{-2}	8.0×10^{-6}	41 s	0.971
9	DBP,61	8	1 [bmim]BF_4	50.1±0.5	2.0×10^{-5}-8.0×10^{-3}	1.0×10^{-5}	45 s	0.969
10	DBP,60	8	2 [bmim]BF_4	53.3±0.6	8.0×10^{-6}-1.0×10^{-2}	7.5×10^{-6}	40 s	0.981
11	DBP,60	8	2 [bmim]PF_6	57.5±0.4	5.3×10^{-6}-1.0×10^{-2}	4.5×10^{-6}	34 s	0.997
12	DBP,59	8	3 [bmim] PF_6	55.3±0.5	8.0×10^{-6}-1.0×10^{-2}	8.0×10^{-6}	38 s	0.985
13	DBP,60	8	2 [omim]PF_6	51.4±0.5	5.0×10^{-5}-1.0×10^{-2}	7.5×10^{-6}	38 s	0.982
14	DBP,68	0	2	4.1±0.7	5.0×10^{-4}-1.0×10^{-3}	5.0×10^{-4}	2 min	0.653

*The results are based on five replicate measurements.

As it can be seen from Table 1, a blank membrane, the membrane without the ion-pair compound, responds too poor (membrane no. 14). As a conclusion, membrane no. 11 which showed the best Nernstian slope (57.5±0.4 mV per decade) was selected. This membrane composition was used for further studies.

3.2. Calibration Graph and figure of merits

The potential response of the electrochemical cell in different concentrations of the Clenbuterol hydrochloride (one decade difference; from 1.0×10^{-8}-1.0×10^{-1} mol L^{-1}) was recorded. According to the Nernst equation, the potential *vs.* –log [Clenbuterol] was plotted as shown in Figure 3. The linear part of the curve (calibration graph) indicates the linear range of the sensor. Drug concentration measurements could be performed in this lower range, but it should be noted that for a more precise analysis more closely spaced calibration points are required. In most of the sensors, the measuring range can extend from 1 molar to 10^{-5} or even 10^{-6} mol L^{-1} [44-50]. The slope of the linear part of the sensor which is 57.5 mV per decade of the Clenbuterol concentration shows a Nerstian behavior and confirms the performance of the proposed sensor. Standard deviation of five replicate measurements was then calculated ±0.4 mV. A linear response towards the Clenbuterol concentration was from 5.3×10^{-6}-1.0×10^{-2} mol L^{-1}. By extrapolating the two segments of the calibration curves, detection limit of the PVC membrane sensor was obtained 4.5×10^{-6} mol L^{-1}.

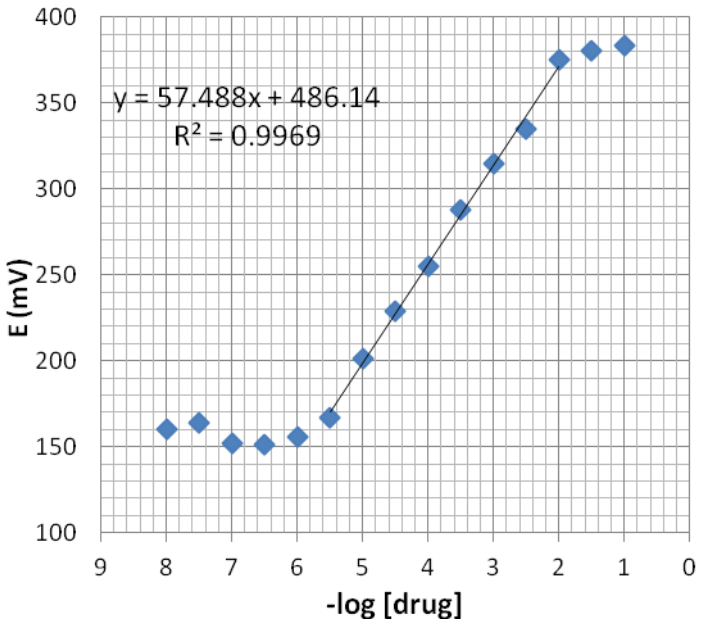

Figure 3. Calibration curve of Clenbuterol PVC membrane sensor; the results are based on 5 replicate measurements.

3.3. Dynamic Response Time

Dynamic response time is the required time for the sensor to achieve values within ±1 mV of the final equilibrium potential, after successive immersions in the sample solutions [51-54]. Its calculation involved the variation and the recording of the Clenbuterol concentration in a series of solutions from 1.0×10^{-5} to 1.0×10^{-2} mol L^{-1}. Sensor was able to quickly reach its equilibrium response in the whole concentration range. This time for the liquid membrane sensor was about 34 s in the concentrated solutions.

3.4. pH Effect on the Sensor Response

To examine the effect of pH on the sensor responses, the potential was measured at specific concentration of the Clenbuterol solution (1.0×10^{-3}, 1.0×10^{-4} and 1.0×10^{-5} mol L^{-1}) from the pH value of 1.0 to 10.0 (concentrated NaOH or HCl solutions were employed for the pH titrations). The results showed that the potential remained constant despite the pH change in the range of 3.0 to 6.0, which indicates the applicability of this electrode in the specified pH range.

Relatively noteworthy fluctuations in the potential *vs.* pH behavior took place below and above the formerly stated pH limits. In detail, the fluctuations above the pH value of 6.0 might be justified by removing the positive charge on the drug molecule and decrease the solubility of the drug in aqueous solution. Fluctuations below the pH value of 3.0 were caused by removal of the membrane ingredients or analyte in the solution.

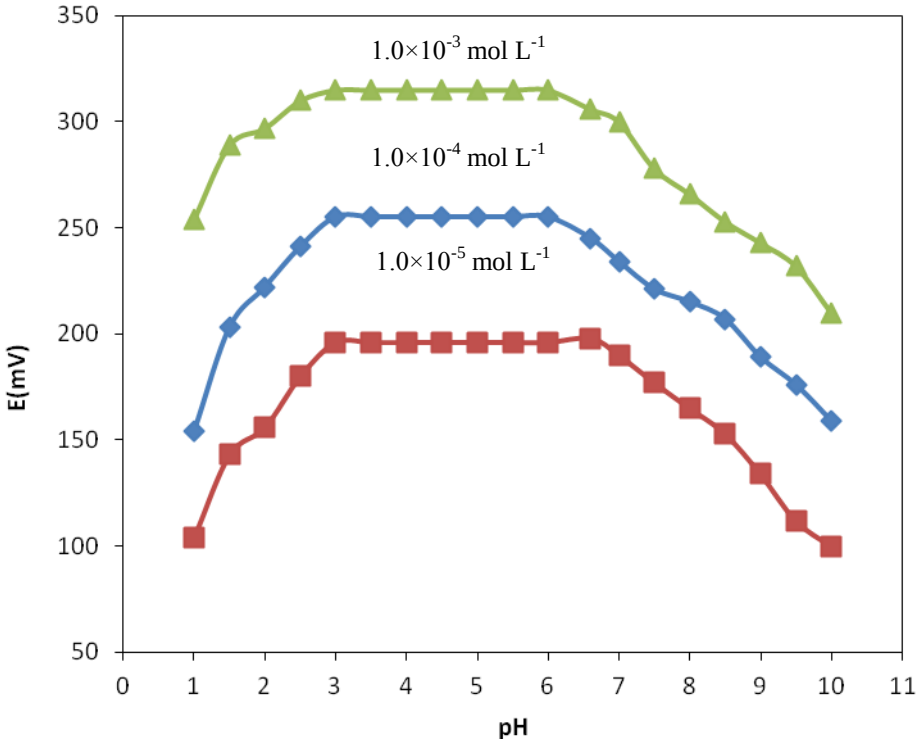

Figure 4. Applicable pH of the electrodes in the test solution of 1.0×10^{-3}, 1.0×10^{-4} and 1.0×10^{-5} mol L^{-1}

3.5. Life-time Study

Sensor lifetime was estimated by the calibration curve, periodical test of a standard solution and calculation of its response slope. For this estimation, three electrodes were employed extensively (1 hour per day) for 10 weeks. The average lifetime for the reported potentiometric sensors is in the range of 4–10 weeks [44-49]. Table 3 shows the results of the lifetime study.

Table 3. Lifetime of PVC membrane electrode

Week	Slope (mV per decade)	DL (mol L^{-1})
First	57.5±0.4	4.5×10^{-6}
Second	57.7±0.4	4.7×10^{-6}
Third	57.4±0.4	5.5×10^{-6}
Fourth	57.1±0.5	7.0×10^{-6}
Fifth	56.8±0.4	9.0×10^{-6}
Sixth	56.2±0.5	1.5×10^{-5}
Seventh	55.7±0.5	3.0×10^{-5}
Eighth	40.4±0.6	8.0×10^{-5}
Ninth	25.9±0.5	3.5×10^{-4}
Tenth	20.4±0.6	7.0×10^{-3}

As can be seen, after 7 weeks utilization of the sensor, a slight gradual decrease in the slope and an increase in the detection limit were observed. It is well known that the loss of plasticizer, sensing element, or ionic site from the polymeric film due to leaching into the sample solution after several times of usage, is a primary reason for limited lifetimes of the sensors. Using RTILs in the composition of the membrane causes a longer lifetime of the sensor.

3.6. Analytical Performance of the Sensor

The proposed sensor was successfully applied for the determination of Clenbuterol in pure solution and in pharmaceutical formulation. Linearity, limit of detection, recovery test, selectivity, precision, accuracy, and ruggedness/robustness were the parameters used for the method validation.

The proposed sensor was evaluated by measuring the drug concentration in some pharmaceutical formulations (Table 4). The drug concentration was determined using calibration method. The results are in satisfactory agreement with the labeled amounts and HPLC standard method.

Selectivity is the most important characteristic of these devices. it is described as an ion-selective electrode specificity toward the target ion in the presence of interfering ions. The potentiometric selectivity coefficients of the Clenbuterol sensor were evaluated by the matched potential method (MPM) [51-54]. The resulting values of the selectivity coefficients are shown in Table 5. Note that all selectivity coefficients shows that the interferences negligible in the performance of the electrode assembly.

Table 4. Potentiometric determination of Clenbuterol hydrochloride in pharmaceutical formulations

Sample	Labeled amount (µg/tab.)	Found by the sensor* (µg/tab.) n=5	standard method n=5	t-test (p-value: 0.05; $t_{theoritical}$: 2.31)
Sample 1	40	38.33±0.57	38.56±0.23	$t_{experimental}$= 2.23
Sample 2	40	37.93±0.72	37.65±0.28	$t_{experimental}$= 2.24
Sample 3	40	41.32±0.45	40.92±0.39	$t_{experimental}$= 2.29

* The results are based on five replicate measurements.

Table 5. Selectivity coefficients of various interfering compounds for Clenbuterol sensor

Interfering ion	Log (K_{MPM})
Na^+	-3.3
K^+	-3.0
NH_4^+	-2.8
Ca^{2+}	-3.2
Mg^{2+}	-3.5
Cl^-	-3.6
NO_3^-	-4.1
Lactose	-4.5
Glucose	-4.3

For repeatability experiment, 3 standard synthetic samples were measured. The RSD values by PVC membrane were 2.71, 3.12 and 3.44%. For ruggedness of the methods a comparison was performed between the intra- and inter-day assay results for Clenbuterol obtained by two analysts.

The RSD% values for the intra- and inter-day assays in the cited formulations performed in the same laboratory by two analysts did not exceed 4.2%. On the other hand, the robustness was examined while the parameter values (pH of the solution and the laboratory temperature) changed slightly. Clenbuterol recovery percentages were good under most conditions, and not showing any significant change when the critical parameters were modified.

4. CONCLUSIONS

A potentiometric PVC membrane sensor was made for determination of Clenbuterol hydrochloride in its pharmaceutical formulation. The sensor demonstrated advanced performance with a fast response time, a lower detection limit of 4.5×10^{-6} mol L^{-1} for PVC membrane electrode and

potential responses across the range of 5.3×10^{-6}-1.0×10^{-2} mol L^{-1}. Sensor respond based on ion-exchange mechanism. The best membrane sensor performance was achieved by a membrane composition of 30% PVC, 60% DBP, 2% RTIL and 8% ion-pair complex. Using ionic liquids in the membrane component improve the performance of the sensor.

ACKNOWLEDGEMENT
The authors are grateful to the Research Council of University of Tehran for the financial support of this work.

References

1. A. Baronti, A. Grieco, C. Vibelli, *Int. J. Clin. Pharmacol.* 18 (1980) 21
2. G.S. Lynch, J.G. Ryall, *Physiol. Rev.* 88 (2008) 729
3. L. Salleras, A. Donguez, E. Mata, J.L. Taberrer, I. Moro, P. Salva, *Public Health Rep.* 110 (1995) 338
4. J.F. Navarro-Martinez, *Lancet*, 336 (1990) 1311
5. G. Brambilla, T. Cenci, F. Franconi, R. Galarini, A. Macri, F. Rondoni, M. Strozzi, A. Loizzo, *Toxicol. Lett.* 114 (2000) 47
6. X.Z. Zhang, Y.R. Gan, F.N. Zhao, *Anal. Chim. Acta*, 489 (2003) 95
7. C.A. Fente, B.I. Vázquez, C. Franco, A. Cepeda, P.G. Gigosos, *J. Chromatogr. B* 726 (1999) 133
8. L. He, Y. Su, Z. Zeng, Y. Liu, X. Huang, *Animal Feed Sci. Technol.* 132 (2007) 316
9. R.N. Liang, Q. Gao, W. Qin, *Chinese J. Anal. Chem.* 40 (2012) 354
10. C. Gausepohl, G. Blaschke, *J. Chromatogr. B* 713 (1998) 443
11. D. Boyd, P. Shearan, J.P. Hopkins, M. O'Keefe, M.R. Smyth, *Anal. Chim. Acta* 275 (1993) 221
12. H.H.D. Meyer, L. Rinke, I. Dursch, *J. Chromatogr. B* 564 (1991) 551
13. P. Andrea, S. Miroslav, S. Silvia, M. Stanislav, *Sens. Actuators B* 76 (2001) 286
14. B. Bo, X. Zhu, P. Miao, D. Pei, B. Jiang, Y. Lou, Y. Shu, G. Li, *Talanta*, 113 (2013) 36.
15. F. Faridbod, F. Mizani, M. R. Ganjali, and P. Norouzi, *Int. J. Electrochem. Sci*. 8 (2013) 10461.
16. M. Javanbakht, S. E. Fard, A. Mohammadi, M. Abdouss, M. R. Ganjali, P. Norouzi, and L. Safaraliee, *Anal. Chim. Acta* 612 (2008) 65.
17. T. Poursaberi, M. R. Ganjali, and M. Hassanisadi, *Talanta* 101 (2012) 128.
18. M. R. Ganjali, N. Motakef-Kazami, F. Faridbod, S. Khoee, and P. Norouzi, *J. Hazard. Mater.* 173 (2010) 415.
19. V. K. Gupta, M. R. Ganjali, P. Norouzi, H. Khani, A. Nayak, and Shilpi Agarwal, Critical Reviews in Anal. Chem. 41(2011) 282.
20. M. R. Ganjali, T. Razavi, F. Faridbod, S. Riahi, and P. Norouzi, *Curr. Pharm. Anal*. 5 (2009) 28.
21. M. Javanbakht, M. R. Ganjali, P. Norouzi, A. Badiei, A. Hasheminasab, and M. Abdouss, *Electroanal*ysis 19 (2007) 1307.
22. M. R. Ganjali, T. Poursaberi, M. Hosseini, M. Salavati-Niasari, M. Yousefi, and M. Shamsipur, *Anal. Sci*. 18 (2002) 289.
23. H. A. Zamani, M. T. Hamed-Mosavian, E. Hamidfar, M. R. Ganjali and P. Norouzi, *Mater. Sci. Eng. C*, 28 (2008) 1551.
24. V.K. Gupta, A.K. Singh, L.K. Kumawat, *Electrochim. Acta*, 95 (2013) 132.
25. M. R. Ganjali, S. Karimi, S. J. Shahtaheri, and P. Norouzi, *Int. J. Electrochem. Sci.*, 8 (2013) 1999.
26. M. R. Ganjali, Z. Memari, F. Faridbod, and P. Norouzi, *Int. J. Electrochem. Sci.* 3 (2008) 1169.
27. V. K. Gupta, R. Ludwig and S. Agarwal, *Anal. Chim. Acta*, 538 (2005) 213.
28. H. A. Zamani, M. R. Ganjali, P. Norouzi, A. Tadjarodi, and E. Shahsavani, *Mater. Sci. Eng. C*, 28 (2008) 1489.

29. H. A. Zamani, M. Masrournia, H. Mohamadzadeh, M. R. Ganjali, M. Rahimizadeh, and P. Ziaei, *Mater. Sci. Eng. C*, 29 (2009) 976.
30. H. A. Zamani, M. R. Ganjali, P. Norouzi, and M. Adib, *Mater. Sci. Eng. C*, 28 (2008) 157.
31. M. Javanbakht, S. E. Fard, A. Mohammadi, M. Abdouss, M. R. Ganjali, P. Norouzi, and L. Safaraliee, *Anal. Chim. Acta*, 612 (2008) 65.
32. S. K. Srivastava, V. K. Gupta, S. Jain, *Electroanalysis*, 8 (1996) 938.
33. H. A. Zamani, M. Mohammadhosseini, S. Haji-Mohammadrezazadeh, F. Faridbod, M. R. Ganjali, S. Meghdadi and A. Davoodnia, *Mater. Sci. Eng. C*, 32 (2012) 712.
34. A. K. Singh, V. K. Gupta and B. Gupta, *Anal. Chim. Acta*, 1 (2007) 171.
35. H.A. Zamani, M. Nekoei, M. Mohammadhosseini, and M.R. Ganjali, *Mater. Sci. Eng. C*, 30 (2010) 480.
36. H. A. Zamani, G. Rajabzadeh, M. Masrornia, A. Dejbord, M. R. Ganjali, and N. Seifi, *Desalination*, 249 (2009) 560.
37. M. R. Ganjali, L. Naji, T. Poursaberi, M. Shamsipur, and S. Haghgoo, *Anal. Chim. Acta*, 475 (2003) 59.
38. V.K. Gupta, A.K. Singh,M. Al Khayat, Barkha Gupta, *Anal. Chim. Acta*, 590 (2007) 81.
39. V. K. Gupta, A. K. Singh and B. Gupta, *Anal. Chim. Acta*, 575 (2006) 198.
40. M. Hosseini, S. D. Abkenar, M. R. Ganjali and F. Faridbod, *Mater. Sci. Eng. C*, 31 (2011) 428.
41. V. K. Gupta, A. K. Jain, Shiva Agarwal and G. Maheshwari, *Talanta*, 71(2007)1964.
42. M. R. Ganjali, F. Faridbod, P. Norouzi, Application of ionic liquids in Electrochemical Sensors and Biosensors as a chapter of the international book entitled: "Ionic Liquids, Theory and Applications" (2011), INTECH Publisher.
43. M. R. Ganjali, H. Khoshsafar, A. Shirzadmehr, M. Javanbakht, and F. Faridbod, *Int. J. Electrochem. Sci.* 4 (2009) 435.
44. M. Shamsipur, S. Rouhani, H. Shaghi, M. R. Ganjali, and H. Eshghi, *Anal. Chem.* 71 (1999) 4938.
45. M. R. Ganjali, P. Norouzi, A. Atrian, F. Faridbod, S. Meghdadi, M. Giahi, *Mater. Sci. Eng. C*, 29 (2009) 205.
46. V. K. Gupta, R. Mangla and S. Agarwal, *Electroanalysis*, 14 (2002) 1127.
47. H. A. Zamani, M. R. Ganjali, H. Behmadi, and M. A. Behnajady, *Mater. Sci. Eng. C*, 29 (2009) 1535.
48. A. K. Jain, V. K. Gupta, L. P. Singh, P. Srivastava and J. R. Raisoni, *Talanta*, 65 (2005) 716.
49. M. R. Ganjali, P. Norouzi, F. S. Mirnaghi, S. Riahi, and F. Faridbod, *IEEE Sensors* J 7 (2007) 1138.
50. H. A. Zamani, M. Rohani, A. Zangeneh-Asadabadi, M. S. Zabihi, M. R. Ganjali, and M. Salavati-Niasari, *Mater. Sci. Eng. C*, 30 (2010) 917.
51. H. A. Zamani, M. R. Ganjali, P. Norouzi, and S. Meghdadi, *Anal. Lett.* 41 (2008) 902.
52. H. A. Zamani, J. Abedini-Torghabeh, and M. R. Ganjali, *Electroanalysis* 18 (2006) 888.
53. H. A. Zamani, A. Arvinfar, F. Rahimi, A. Imani, M. R. Ganjali and S. Meghdadi, *Mater. Sci. Eng. C*, 31 (2011) 307.
54. H. A. Zamani, M. R. Ganjali, and M. J. Pooyamanesh, *J. Brazil Chem. Soc.* 17 (2006) 149.