Int. J. Electrochem. Sci., 11 **(2016)** 6761 – 6774, doi: 10.20964/2016.08.14

International Journal of ELECTROCHEMICAL SCIENCE
www.electrochemsci.org

Two Novel Potentiometric Sensors for Determination of Clonidine in Some Pharmaceutical Formulation

H. AlRabiah[1], A. Al-Majed[1], M. Abounassif[1] and G.A.E.Mostafa[1,2,]*

[1] Pharmaceutical Chemistry Department, College of Pharmacy, King Saud University, P.O.Box 2457, Riyadh11451, Saudi Arabia
[2] Micro-analytical Lab., Applied organic Chemistry Department, National Research Center, Dokki, Cairo, Egypt
[*]E-mail: gamal_most@yahoo.com

Received: 27 April 2016 / *Accepted:* 29 May 2016 / *Published:* 7 July 2016

Two novel membrane sensors with cylindrical configuration for clonidine HCl have been developed. The electroactive material incorporate β- or γ- cyclodextrin as ionophores. Sensor 1 and 2 were fabricated utilizing β- and γ- cyclodextrin in presence of potassium tetrakis (4-chlorophenyl)borate (KTpClPB) as ion additive , PVC as matrix and o-nitrophenyl octyl ether (o-NPOE) as plasticizer. Both sensors showed a significant response to clonidine with near-Nernstian cationic slope of 53 and 54 mV/ decade over a relative wide dynamic range of 1×10^{-2} - 6.0×10^{-6} and 1×10^{-2} - 5.5×10^{-6} M, for sensor1 and 2 respectively. The detection limits were 5×10^{-6} and 3.5×10^{-6} M for sensor 1 and 2 in the pH range of 2-7. The developed sensors using the novel ionophores were improve the selectivity for clonidine in presence of different ions. The determination of 230.09 μg/ml of clonidine show good accuracy and precision (101.99 and 10.89% and 2.77 and 3.36% respectively) for sensor β- and γ-CD, respectively. The investigated sensors have been connected for determination of clonidine in its dosage form and contrasted with those got utilizing the HPLC technique. The sensors have been used as pointer sensors for determination of clonidine by potentiometric titration. The investigated sensors revealed good analytical characteristics include, high selectivity, fast response, long life time, good stability with high accuracy and precise .

Keywords: Clonidine HCl, β- and γ- cyclodextrin, ionophore , Potentiometry

1. INTRODUCTION

Clonidine is used to treat high blood pressure and the treatment of attention deficit and an increase in activity and anxiety disorders, migraine and menopause, diarrhea, some cases of pain and is also used for the treatment of addiction and smoking materials, soft and opiates [1]. It is considered as

a centrally acting α_2 adrenergic agonist and imidazole receptor agonist that has been in clinical use since many years ago [2]. Its chemical structure is shown in Figure 1 [3].

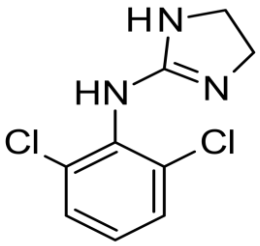


Figure 1. Chemical structure of clonidine

Spectrofluorimetry [6], high performance liquid chromatography-ultraviolet (HPLC-UV)[7, 8], HPLC-Mass detection [9-11] and gas chromatography-mass detection [12]. However, most of these techniques involve time consuming, sophisticated instruments, complicated procedure, high price instruments and need a high qualified person.

On the other hand, PVC membrane sensors as analytical tools are characterized by cheap and portable instruments. PVC membrane sensors are simple, rapid, sensitive, economical, applied in different areas [13-15].

Only one potentiometric membrane sensor for clonidine has been reported [16]. The published method involves clonidine-tetraphenylborate ion-associate complex (electroactive substance) as PVC sensor for clonidine [16]. The present investigation is completely studies compared with the reported method, nearly all the validation results not including [16]. Moreover the measurement was in aqueous solution without any control of the pH [16]. The proposed method was carried out in controlled pH value (2.0- 7.0) and the best pH value was acetate buffer of pH 5.0. As a result our methods are more robust than published procedure.

Cyclodextrins are known to form inclusion complex with many different substances e.g. organic and inorganic compounds, which form stable complexes (host-guest interaction) [17, 18]. Cyclodextrins are very important class of organic compound with large size of cavity that is used in electrochemical studied. Preparation of PVC membrane sensors using large cavity of compound for example cyclodextrin modified electrodes is a new field of research area for electrochemical sensors especially in drug analysis [19-21].

Cyclodextrins been previously reported as electro-active materials in potentiometric PVC sensor for the determination of many compounds, for example some quaternary ammonium drugs [20], fluorinated surfactant [22], protonated amine [23], and chiral molecules [24].

To the best of our knowledge, this is first time to using cyclodextrin as ionophore to determination of clonidine in its pharmaceutical formulation. The present work offered two novel ion selective membrane sensors for clonidine. Sensor 1 is based on β-cyclodextrin and sensor 2 is based on γ-cyclodextrin as sensing material (ionophore) to construct PVC sensors to determine clonidine in its dosage form.

2. METHOD

2.1. Apparatus

A WTW pH/mV meter (523) utilizing clonidine PVC sensors (working electrode) joined with an Orion Ag/AgCl reference electrode (90-02) containing saturated solution of potassium nitrate in the external compartment were utilized. A combined Ross glass pH electrode (Orion 81-02) might have been utilized for measurement of pH. All potentiometric estimations were constructed on during room temperature.

2.2. Reagents and materials.

High molecular weight polyvinyl chloride powder (PVC), dioctyl phthalate (DOP), dibutyl sebacate (DBS), o- NPOE, tetrahydrofuran (THF) for purity > 99 % were got from Aldrich Chemical compound. Clonidine HCl might have been buy from sigma chemical compound. Potassium tetrakis (4-chlorophenyl)borate (KTpClPB), β-CD and γ-CD, were got from BDH, compound Ltd. Catapres® tablets containing 0. 1 mg about clonidine HCl. Acetate buffer solution of pH 5 might have been prepared utilizing mixture of 0. 05M of sodium acetate and acetic acid. All reagents were analytical reagent grads and deionized water might have been utilized.

2.3. Preparation of standard solution.

The standard stock of 1×10^{-2} M solution clonidine was prepared by dissolving the exact quantity of clonidine in double distilled water. Series of standard clonidine solutions were prepared covering the range of 1×10^{-2} - 1×10^{-6}M by suitable dilution.

2.4. Fabrication of clonidine.

In glass Petri dish (5 cm diameter), five mg of β- or γ-cyclodextrin and five mg of potassium tetrakis(4-chlorophenyl)borate were mixed well with 190 mg PVC powder, 0.350 ml of DOP or DBS or NPOE. The mixture was dissolved in about 3 ml THF. The sensing membranes have been made, after the solvent has been allowed to evaporate over night at room temperature. A polyethylene tube with suitable parameters was stuck with a plate of 10 mm film of PVC layer utilizing THF. Electrode bodies were utilized to which the polyethylene tube is appended toward one side. The inside reference arrangement (level with volumes of 1×10^{-2} M of clonidine and potassium chloride) [25, 26] was utilized to document the electrode body. Internal reference electrode of Ag/AgCl was utilized. The indicator sensors were soaked in clonidine for suitable time period (in any event for 1 hr) and after measurement the electrode was kept in the same solution.

2.5. Procedure

The clonidine sensors were calibrated by insert the working electrode in combined with the reference electrode in a 50 ml measuring cell containing 9.0 ml of acetic acid of pH 5.0. At that point 1.0 ml aliquot of clonidine arrangement was inserted and permitted to equilibrate with nonstop stirring, to give last clonidine concentration range from 1×10^{-2} to 1×10^{-6}M. The potential was recorded after adjustment to the final reading and the calibration graphs were performed by plotting the recorded potential as an element of the negative logarithm of clonidine concentration. The subsequent charts were utilized for resulting determination of obscure clonidine

2.6. Determination of clonidine in its dosage form

Ten tablets of catapres® tablets (0.1mg each of clonidine) were accurately weighed, pulverized to give a fine powder. An appropriate amount of powder equivalent to 0.1 mg of clonidine was transferred to a 100 ml beaker and dissolved in water, sonication for about 10 min. Transferred suitable aliquot of that solution into 100 ml measuring flask after filtration, pH was controlled using acetate buffer (pH 5), then completed to the mark with double distilled water. The potentiometry of the arrangement was measured utilizing the proposed PVC-sensors. The potentiometry was recorded after the sign adjustment (± 0.5 mV/min) and the concentration was computed from the past alignment diagram under indistinguishable exploratory condition.

Reconstituted powder was prepared by addition of known amount of clonidine powdered (0.1 mg) with the other components present in tablet formulation. The concentration of clonidine in the previous solution was assayed using the proposed procedure.

3. RESULTS AND DISCUSSION

3.1. Response mechanism of the proposed sensors

The inclusion complexation and the molecular recognition are of important concern in host-guest chemistry which offers an excepted methodology to chemical sensing. The potentiometric sensors based on ionophore is typically controlled by the molecular communication capacity between guest (analyte) and the host particle (cyclodextrin)[27, 28].

Beta-and γ -cyclodextrin can shape a consideration complex with numerous guest particles, for example, clonidine, in light of the fact that its pit is outside hydrophilic and in-side is hydrophobic, which permit to frame entry point complex. The inclusion mechanism are based on different forces e.g. formation of hydrogen bonds, hydrophobic interactions and van der Waals force [27,28]. The chemical structure of β- and γ-cyclodextrin and clonidine are shown in Fig.2

It was found that addition potassium tetrakis(4-chlorophenyl)borate as ionic site to the membrane composition of PVC clonidine sensor is an important to get a good Nernstian response and to improve the selectivity of the membrane[29]. Addition of 5 mg of KTpClPB as anion

excluder to the membrane composition was enhancing both selectivity and sensitivity of the proposed sensors.

The mechanism of the investigated sensors containing either β-or γ- cyclodextrin ionophore as electro-active material is based on the formation of inclusion complex, where the complex is based on different forces [27, 28].

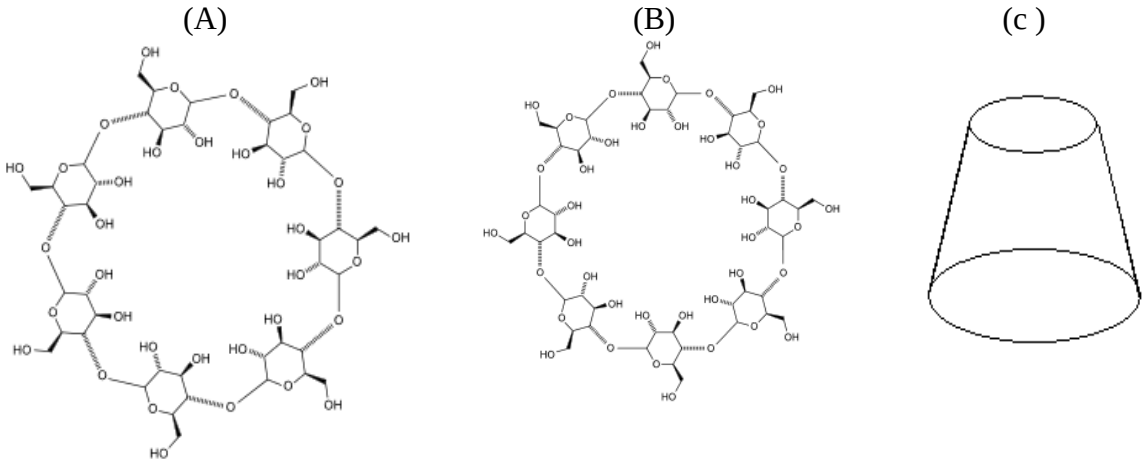


Figure 2. Structure (A) , (B) and (C) are β- and γ-cyclodextrin , toroidal shape.

3.2. Effect of membrane plasticizer.

Clonidine ion-selective membrane sensors have been investigated using three different plasticizers, in order to check their analytical characteristic in various plasticizers. The obtained ionophores combined with three plasticizer, dibutyl phthalate (DBP), dioctyl phthalate (DOP) and o-NPOE were tested. It is surely understood that the development of PVC membrane sensor required the utilization of a plasticizer which goes about as a fluidizer permitting homogenous disintegration and dispersion portability of the ionophore through the membrane [30]. PVC membrane sensor of β-, or γ-cyclodextrin with two plasticizer (DOP or NPOE) was observed to be suitable as plasticizer and ideal accessible and available mediators for clonidine sensors. The best results were found with DOP as available mediator for sensor 1 and sensor 2. Thus dioctyl phthalate was used for the present work, as plasticizer.

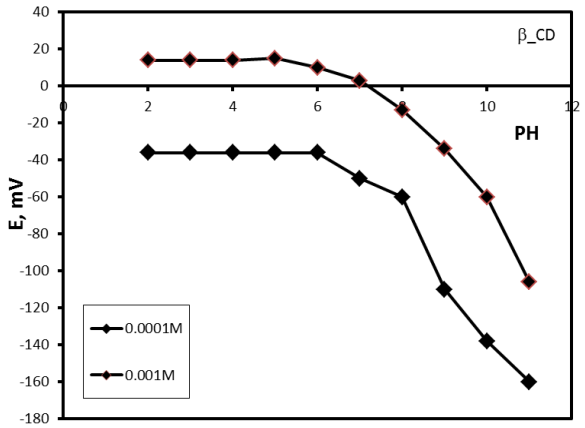
3.3. Influence of pH and the response time.

The effect of pH on various clonidine concentrations was studied at distinctive pH ranges to achieve the ideal trial condition. The pH of the measuring arrangement was balanced utilizing weak solution of hydrochloric or sodium hydroxide. The clonidine - PVC sensor was tested into clonidine concentration of 0.001 and 0.0001M. The pH profile demonstrates that the slope of the investigated sensors is consistent (~ 53 or 54 for sensor 1 and 2, separately) in the pH scope of 2 - 7 (Fig.3). At higher pH (pH > 7), (pKa =8.05)[3] the 0.001M potential diminished because of the steady increment

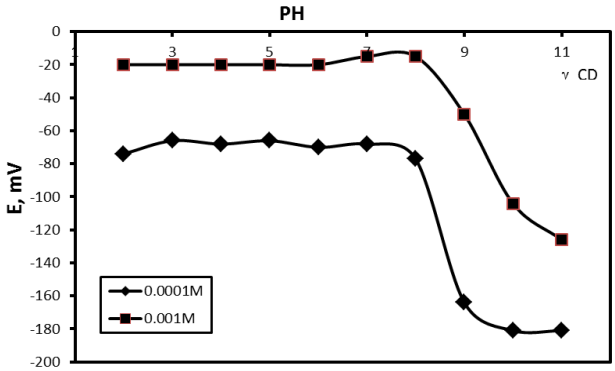
in the concentration of the un-protonated types of clonidine. Subsequently the pH range from 2-7 was thought to be the most suitable pH range for the two sensors.

Average response time [31] is minimum time period required for the electrode potential to achieve a stable potential reading of the last harmony perusing. After measuring the electrode potential in distinctive clonidine concentration utilizing either increment or diminish as a part of concentration of clonidine.

The electrode response was noticed to be 20s for concentration of ≥ 0.001and 35s for concentration ≤ 0.0001M. Everyday reproducibility of the sensor is about ±0.5 mV for the same arrangement. The profitable lifetime of the sensor is around 6 weeks, in the midst of which the potential slope is reproducible. Likewise after over one month another area from the main membrane was found to probably suitable with high accuracy.



A



B

Figure 3. Influence of pH on the electrode response A) β-D and B) γ-CD using two different concentration of clonidine.

3.4. Interferences studies

The impacts of diverse effect of organic and inorganic particles on the response of clonidine sensors were inspected. The potentiometric selectivity coefficients $K_{A,B}^{pot}$ were estimated according

IUPAC guidelines utilizing separate solution or mixed solution method [31, 32] using acetate buffer of pH 5. The results of selectivity coefficient are listed in Table 1. The outcomes are in Table 1, which the selectivity coefficient was low show that the proposed technique was free from the interference of the investigated ions.

Table 1. Selectivity coefficients of clonidine -PVC sensors.

Interferent, B	$K^{Pot}_{cloni.,B}$ Sensor 1	$K^{Pot}_{cloni.,B}$ Sensor 2
Na^+	7.1×10^{-3}	1.3×10^{-2}
K^+	1.1×10^{-2}	1.3×10^{-2}
Ca^{2+}	1.0×10^{-2}	1.2×10^{-3}
Zn^{2+}	1.1×10^{-2}	1.5×10^{-3}
Co^{2+}	1.0×10^{-2}	1.3×10^{-2}
Ni^{2+}	7.9×10^{-3}	1.4×10^{-3}
Magnesium Stearate [b]	8.9×10^{-4}	1.3×10^{-3}
Glucose[b]	8.9×10^{-4}	1.3×10^{-3}
Lactose monohydrate[b]	8.9×10^{-4}	1.3×10^{-3}
Starch[b]	8.9×10^{-4}	1.3×10^{-3}
Microcrystalline cellulose [b]	8.9×10^{-3}	2.2×10^{-3}

[b] mixed solution method

3.5. Characteristics of the proposed sensors.

The potentiometric response attributes of the clonidine sensors in view of the utilization of β- or γ-cyclodextrin as ionophore and dioctyl phthalate as a plasticizer in PVC frameworks were assessed by proposed sensors. Results in Table 2 demonstrate the essential qualities of the PVC sensors. The least squares mathematical statements acquired from the calibration graph as follows:

E (mV) = S log [clonidine] + Intercept (1),

where E: electrode potential, S : slope of the electrodes (53.0± 0.5, and 54.0 ± 0.5 mV for

sensor 1 or 2 , respectively) and intercept (149.0 ± 0.6 and 142.0 ± 0.6 for β- or γ- sensor, respectively).

Table 2. Characteristics response of clonidine sensors.

Parameter	Sensor 1	Sensor 2
Calibration range	6.0×10^{-6} -1×10^{-2}	5.5×10^{-6} -1×10^{-2}
Slope, (mV/ decade)	53 ± 0.6	54 ± 0.6
Intercept, mV	149 ± 0.7	60 ± 0.7
Correlation Coefficient, (r)	0.998	0.998
Lower limit of detection (LOD), M	5.0×10^{-6}	3.5×10^{-6}
Lower limit of quantification (LOQ), M	6.0×10^{-6}	5.5×10^{-6}
Response time at 1×10^{-3} M, second	20 ± 0.7	20 ± 0.7
pH range	2 - 7	2 -7

3.6. Validation of the investigated method

3.6.1. Limit of detection and limit of quantification

Each trial in the estimation extent was tried five times. The potentials acquired for the five examinations were found the middle value of at every concentration [33]. The measured potential was plotted against concentration. Logarithmic (equation 1) $X = S$ log [clonidine] $+Y$ *was obtained,* which is the relationship between the potential *and concentration,* where X : potential, S : slope, and Y : intercept and (r) : correlation coefficient. The concentration range was in the range of 1×10^{-2} to 5.8×10^{-6} and 1×10^{-2} to 4.0×10^{-6}M for sensor 1 and 2, individually in the pH range of 2 - 7. The lower limit of detection and lower limit of quantification were resolved agreeing the IUPAC suggestion [31]. The lower limit of detection characterized as the convergence of clonidine comparing to the crossing point of the extrapolated direct fragment of the alignment diagram which is 5×10^{-6} and 3×10^{-6} for sensor 1 and 2 separate(Fig.4)

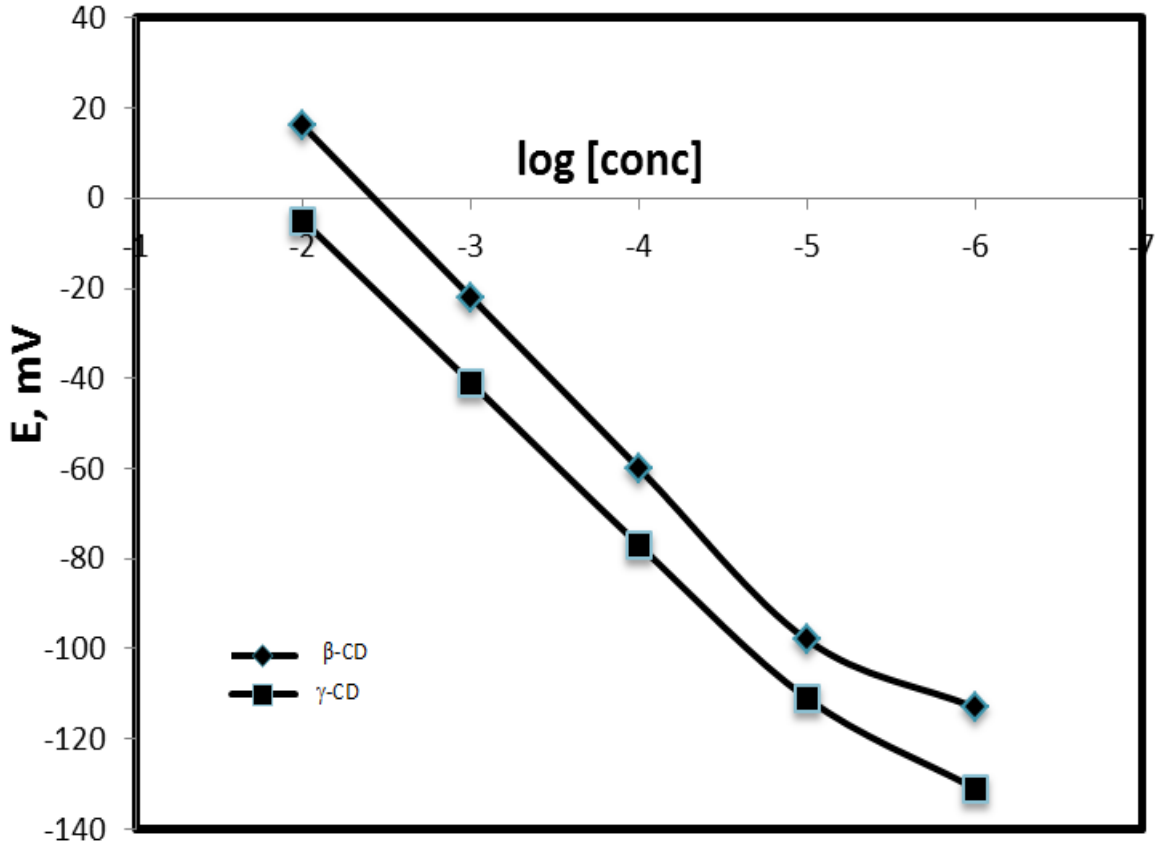


Figure 4. Calibration graphs of clonidine sensors.

3.6.2. Accuracy

The recovery of clonidine were computed by contrasting the deliberate concentration with found by direct included careful in acetate buffer of pH 5.0. The measure of recovery, at every concentration, was registered utilizing the accompanying mathematical statement.

Recovery *(%)* = (found concentration / added concentration) × 100.

The average recovery (accuracy) of 230.09 μg/ml of clonidine was 101.99 and 102.89% for sensor 1 and 2, respectively (Table 3).

3.6.3. Precision

Precision of the assay was examined [33] during that day and in diverse days by the examination of clonidine at 230.09μg/ml in five duplicate over a time of three days. The five repeat were calculated in the intra-day and between day precision. Precision was accounted for as RSD%. The outcomes acquired (Table 3) are inside of the acceptance range of less 3.08 % (accuracy).

Table 3. Accuracy and precision of the proposed PVC membrane sensors.

Parameter	Clonidine (230.09 μg/ml)* Intra day		Clonidine (230.09μg/ml)* Inter days	
	Sensor 1	Sensor 2	Sensor 1	Sensor 2
R, %	101.99	102.89	101.2	101.5
R.S.D, %	2.77	3.36	2.88	3.36
E, %	-1.98	2.9	-1.1	-1.49
Slope	53.0 ± 0.5	54.0 ± 0.5	53.0 ± 0.7	54.0 ± 0.6
Correlation coefficient	0.998	0.997	0.997	0.997

*****E is error %, and n=5.

3.6.4. Ruggedness.

The ruggedness of the proposed strategy was assessed [33] via completing the investigation utilizing two diverse examiner and distinctive instrument on distinctive days. The RSD value was less 3.08% were watched for redundant estimations in three diverse days utilizing two different instruments and administrators. The obtained data reveal that the system is equipped for creating data with high accuracy

3.6.5. Robustness.

The robustness of the investigated PVC sensors is completed by studding the trial parameters that influencing the potential response for example pH and reaction time. Preparatory studied on of the obtained results under these different conditions proposed that the strategy is fairly robust and the main pH variable ought to be in the scope of 2 - 7. The optimum pH was 5 using acetate buffer.

3.7. Application of clonidine-PVC sensors.

The application of clonidine PVC sensors for the assay of clonidine in its dosage form was checked by the examining the recovery of known concentration of clonidine in pure solutions.

The assay of 2.3 - 2300.9 μg/ml clonidine solutions (in five replicate) by the investigated methods show good precision and accuracy using both sensors. Results are presented in the following Table (Table 4).

Table 4. Determinations of clonidine using the proposed procedure.

Added (µg/ml)	Sensor 1 * R%	SD	RSD%	E%	Sensor 2 * R%	SD	RSD%	E%
2.301	100.0	1.53	2.43	0.00	98.9	1.54	1.57	-1.05
23.01	100.0	2.0	1.75	0.00	99.5	1.154	0.90	-0.5
230.09	97.9	2.0	1.48	2.09	99.1	2.88	1.84	-0.91
2300.9	99.0	2.6	0.114	1.04	103.0	2.80	0.11	-2.74

SD: standard deviation, E: error%
* n= 5

Table 5. Determination of clonidine using the clonidine -PVC membrane sensors.

Preparation	Clonidine (nominal, value)	Suggested procedure* Recovery % (RSD, %) Sensor 1	Sensor 2	HPLC Recovery % (RSD, %)
Reconstituted powder	0.1 mg	102.0 (2.67)	103.0(2.88)	97.8 (2.3)
Catapres	0.1 mg	101.8 (2.55)	103.0 (2.75)	98.0 (2.1)

*Average of five determinations.

The application of the clonidine sensors for the determination of clonidine in its dosage form was again tested by study the concentration of an exact amount of clonidine in its synthetic laboratory powder. The accuracy acquired by the propose sensors was show good recovery values (RSD, % was less than 3.08%) utilizing both sensors.

Again, the determination of clonidine in its dosage show a good recovery and relative standard deviation for sensor 1 or 2 , separately . The outcomes are introduced in Table 5.

Results acquired for the investigation of clonidine in its dosage form utilizing the proposed sensors are match with the reported HPLC technique [8], results are given in Table 5. The information got are appeared in Table 5 demonstrates that the proposed PVC sensors show a high level of accuracy and precision compared with HPLC strategy.

3.7.1. Potentiometric titration application.

The developed sensors have been inspected as an end point marker for the assay of clonidine utilizing precipitation titration reaction. Titration clonidine with sodium tetraphenylborate utilizing

sensor 1 and 2 have been inspected (Fig. 5). The results indicate that clonidine react with NaTPB in the molar ratio of 1:1. The titration bends were symmetrical with an exceptionally all around characterized potential jump of around 120 and 150 mV for sensor 1 and 2, individually, demonstrating the high affectability of the sensors.

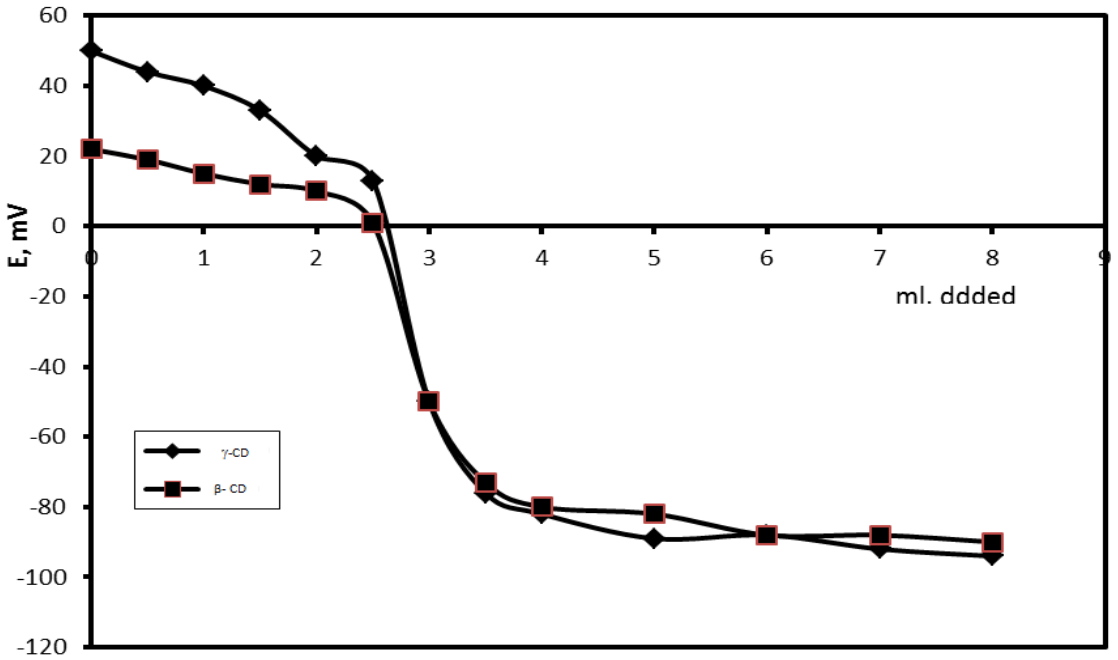


Figure 5. Potentiometric titration curves of 2.5 ml of 0.01 M clonidine with 0.01M Na-TPB using clonidine sensors.

4. CONCLUSION

Two novel potentiometric membrane sensors for clonidine are portrayed and created utilizing two proposed sensors. The proposed sensors depend on utilization of β- or γ-cyclodextrin as neutal ionophore and dioctyl phthalate as a plasticizer and KTpClPB as an anionic excluder in PVC as a polymeric framework. The sensors demonstrate a reproducible, specific and close Nernstian response over a relative wide dynamic range of clonidine for sensor 1 and 2 separately in the pH scope of 2 - 7. Beta-CD sensor show a higher sensitivity compared with γ-CD sensors. The determinations of clonidine show good recovery and relative standard deviation for sensors 1, and 2 separately. The outcomes got are inside of the acceptance range of less than 3.08 % (RSD) and the normal recovery value of 101.1%. The sensors have been utilized as marker electrode for potentiometric titration of clonidine.

ACKNOWLEDGEMENTS
The authors extend their appreciation to the Deanship of Scientific Research at King Saud University for funding the work through the research group project No. RGP-1436-024.

References

1. W. Martindale, S.C. Sweetman, Martindale: the complete drug reference, Pharmaceutical press London, 1999.
2. M. JE Neil, Clonidine: clinical pharmacology and therapeutic use in pain management, *Current clinical pharmacology*, 6 (2011) 280.
3. A.C. Moffat, M.D. Osselton, B. Widdop, E. Clarke, Clarke's analysis of drugs and poisons: in pharmaceuticals, body fluids and postmortem material s. Vol. 1, Pharmaceutical Press, 2004.
4. S.S. Guimaraes, G.D. Sousa, S.G. JÚNIOR, D.M.C. BRANCO, M.M. Albuquerque, B. Leila, D.P. Santana, *Lat. Am. J. Pharm*, 31 (2012) 1222.
5. R.S. Haggag, S.F. Belal, R.A.-A. Shaalan, *Journal of Food and drug analysis*, 19 (2011) 174.
6. F.A. El-Yazbi, M. Bedair, M.A. Korany, *Analyst*, 111 (1986) 477.
7. N. Devanaboyina, B.C. Kumar, B. Vijay, M. Bhanu, V. Gayathri, *Journal of Atoms and Molecules*, 2 (2012) 93.
8. S.M. Walters, D.B. Stonys, *Journal of chromatographic science*, 21 (1983) 43.
9. J. Zhuang, J. Chen, X. Wang, Y. Pang, H. Bi, L. Huang, G. Zeng, X. Liao, Z. Ma, X. Chen, *Biomedical Chromatography*, (2015).
10. R. Nirogi, V. Kandikere, K. Mudigonda, P. Komarneni, *Biomedical Chromatography*, 22 (2008) 992.
11. G. Ke, E. Zhang, L. Wang, Q. Zhang, H. Du, H. Guo, Acta pharmaceutica Sinica, 39 (2004) 367-369.
12. T. Wenzl, E.P. Lankmayr, R. Wintersteiger, A. Sadjak, R. Likar, D. Zakel, *Journal of biochemical and biophysical methods*, 53 (2002) 131.
13. M.K. Bojdi, M.H. Mashhadizadeh, M. Behbahani, A. Farahani, S.S.H. Davarani, A. Bagheri, *Electrochimica Acta*, 136 (2014) 59.
14. M.K. Bojdi, M. Behbahani, A. Sahragard, B.G. Amin, A. Fakhari, A. Bagheri, *Electrochimica Acta*, 149 (2014) 108.
15. M.K. Bojdi, M. Behbahani, M.H. Mashhadizadeh, A. Bagheri, S.S.H. Davarani, A. Farahani, *Materials Science and Engineering: C*, 48 (2015) 213.
16. M.R. Ganjali, S. Karimi, S.J. Shahtaheri, P. Norouzi, , *Int. J. Electrochem. Sci*, 8 (2013) 1999.
17. E.M. Del Valle, *Process biochemistry*, 39 (2004) 1033.
18. A.R. Hedges, Industrial applications of cyclodextrins, *Chemical Reviews*, 98 (1998) 2035.
19. R. Yang, K.a. Li, K. Wang, F. Zhao, N. Li, F. Liu, *Analytical chemistry*, 75 (2003) 612.
20. A.M. El-Kosasy, M. Nebsen, M.K.A. El-Rahman, M.Y. Salem, M.G. El-Bardicy, *Talanta*, 85 (2011) 913.
21. M. Trojanowicz, *Electrochemistry Communications*, 38 (2014) 47.
22. S.R. Patil, M. Turmine, V. Peyre, G. Durand, B. Pucci, *Talanta*, 74 (2007) 72-77.
23. A.M. El-Kosasy, *Journal of AOAC International*, 86 (2003) 15.
24. K.I. Ozoemena, R.-I. Stefan, *Talanta*, 66 (2005) 501.
25. S.S. Hassan, S.A. Marzouk, , *Talanta*, 41 (1994) 891.
26. A. Carggs, G. Moody, J. Tomas, *J. Chem. Educ*, 51 (1974) 541.
27. K.-H. Frömming, J. Szejtli, Cyclodextrins in pharmacy, Springer Science & Business Media, 1993.
28. R. Challa, A. Ahuja, J. Ali, R. Khar, *Aaps Pharmscitech*, 6 (2005) E329.
29. R. Eugster, P.M. Gehrig, W.E. Morf, U.E. Spichiger, W. Simon, *Analytical chemistry*, 63 (1991) 2285.
30. M.B. Gholivand, M. Mohammadi, M. Khodadadian, M.K. Rofouei, *Talanta*, 78 (2009) 922.
31. R.P. Buck, E. Lindner, Recommendations for nomenclature of ionselective electrodes (IUPAC Recommendations 1994), Pure and Applied Chemistry, 66 (1994) 2527-2536.

32. Y. Umezawa, P. Bühlmann, K. Umezawa, K. Tohda, S. Amemiya, Potentiometric selectivity coefficients of ion-selective electrodes. Part I. Inorganic cations (technical report), *Pure and Applied Chemistry*, 72 (2000) 1851.
33. J.N. Miller, J.C. Miller, Statistics and chemometrics for analytical chemistry, Pearson Education, 2005.