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Preparation and Characterization of an Atenolol Selective Electrode Based on a PVC Matrix Membrane

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Atenolol selective electrodes were prepared based on a complex atenolol-phosphotungstate as an active material using the plasticizers di-butyl phosphate (DBP), tri-butyl phosphate (TBP), o-nitro phenyl octyl ether (NPOE) and di-octyl phthalate (DOPH) in a PVC matrix membrane. The properties of the prepared electrodes were studied, namely slope, concentration range, detection limit, lifetime, pH effect and selectivity. The experimental results showed that the best electrode was based on DOPH as plasticizer, displaying a linear range from 1.00 x 10^{-4} M to 5.00 x 10^{-2} M with a Nernstian slope of 55.91 mV/decade and correlation coefficient of 0.9995. The detection limit was 5.00 x 10^{-5} M and the lifetime was around 90 days. The proposed electrode was successfully applied to the determination of atenolol in a pharmaceutical preparation. The average recovery for atenolol determination in tablets was around 98.50%, with standard deviation ± 0.1.

Key Words: Atenolol selective electrode, atenolol determination, phosphotungstic acid, plasticizers.

Introduction

Ion-selective electrodes (ISEs) are one of the most frequently used potentiometric sensors in laboratory analysis as well as in industry, process control, physiological measurements, environmental monitoring and drug analysis. Atenolol, (RS)-4-(2-hydroxy-3-isopropylaminopropoxy)phenylacetamide, $C_{14}H_{22}N_2O_3$, is a white powder used commonly in the treatment of arterial hypertension, angine pectoris and cardiac arrhythmias.[1,2] The most common method used in atenolol determination is liquid chromatography,[3] which has been developed by Rapado-Martinez et al.[4] for the simultaneous determination of metoprolol, oxperenolol, amiloride and vasodilator hydralazine in pharmaceutical drugs. An assay of the orally administrated hypertension drugs atenolol, amilodipine, nifidipine and other drugs was described by Sundaresan et al. [5] using HPLC.

A new simple, precise, accurate and rapid performance thin layer chromatographic method have been developed for simultaneous determination of atenolol in pharmaceutical dosage forms, the percentage recovery was 101%. [6] A second derivative spectrophotometric method for the simultaneous determination of atenolol and nifedipine in dosage forms was developed by Umapathi[7]. Ion-selective electrodes play an important role in pharmaceutical analysis [8] due to their simplicity, rapidity and accuracy. A novel ion

selective PVC membrane electrode for the determination of propranolol was developed by Aboul-Enein and Sun; [9] they used silicotungstic acid as a counter ion with diisononyl phthalate as plasticizer. The electrode was successfully used for the analysis of propranolol in a pharmaceutical formulation with recoveries of 99.2%-102.6%. Methacycline ion-selective PVC membrane electrodes were also developed by Eboul-Enein et al.[10] based on the use of methacycline-tetraphenylborate as the electroactive substance, and di-octyl phthalate as plasticizer. The electrode was successfully applied for the determination of methacycline hydrochloride in pharmaceutical tablets by a direct potentiometric method. An ion-selective membrane electrode for ketamine hydrochloride has been constructed by Alizadeh and Mehdipour,[11] using a modified PVC membrane and o-nitropenyl octyl ether as plasticizer. The electrode was applied for ketamine determination and used to study the interaction of bovine serum albumin with ketamine in phosphate buffer.

In the present study, we constructed and characterized several electrodes for the potentiometric determination of atenolol. The membranes consisted of atenolol-phosphotungstate as an active material with different plasticizers. The electrode parameters were investigated via potentiometric measurements including direct, standard addition and titration methods.

Experimental

Equipment

1. Expandable ion analyzer, Orion model EA 940 for potential measurements, Switzerland.
2. Calomel reference electrode type Metrohm, Switzerland.
3. Combined glass electrode type Orion 91 – 02, Swiss made.
4. The electrode used for atenolol was home constructed according to reference 12, as follows: The Ag-AgCl electrode and 0.1 M atenolol solution were used as the reference electrode and the internal filling solution of the electrode, respectively. One side of a piece of PVC tube (1-2 cm long) was flattened and smoothed by placing it on a glass plate moistened with THF. A disk of the membrane was cut equal to the external diameter of the PVC tubing and mounted on the polished end. The other side of the PVC tubing was then connected to the electrode body. The assembled electrodes were conditioned by soaking in 0.1 M atenolol solution for at least 3 h before the use of the electrodes.

Chemicals

1. Atenolol standard and tenordine tablets (50 mg atenolol) were a gift from the state company of drug industries and medical appliances (IRAQ-SDI -Samara). Novaten tablet, 100 mg atenolol (Ajanta Pharma, India) and Ateno tablet, 100 mg atenolol, (international pharmaceutical industries company EICO, Egypt) were obtained from local pharmacies.
2. Plasticizers, di-butyl phosphate (DBH), tri-butyl phosphate (TBP), o-nitro phenyl octyl ether (NPOE) and di-octyl phthalate (DOPH) were obtained from Fluka AG. Other chemicals and reagents of analytical grade quality were obtained from Fluka , BDH and Aldrich.

Standard solutions

1. Standard solution of 0.1 M atenolol was prepared by dissolving 1.3315 g of standard atenolol in a small amount of ethanol and the volume was made up to 50 mL with water.

2. Stock solutions of 0.01 M of each of $NaNO_3$, KCl, LiBr, $BaCl_2$, $MnSO_4$, and $CdSO_4$were prepared; other standard solutions were prepared by subsequent dilution of the stock solutions.

All solutions were prepared using doubly distilled deionized water.

Preparation of ion-pair compound

The ion-pair of atenolol-phosphotungstate (A-PT) was prepared by mixing 20 mL of 0.01 M solution of atenolol with 25 mL of 0.01 M phosphotungstic acid with stirring. The resulting precipitate was filtered off, washed with water, and dried at 60 °C.

Casting the membrane

Atenolol matrix was immobilized into the PVC matrix membrane as described by Davis et al.[13] A-PT (0.04 g) was mixed with 0.36 g of plasticizers: DBP (electrode I), TBP (electrode II), NPOE (electrode III), or DOPH (electrode IV). Then 0.17 g of PVC powder was sprinkled on 6 mL of THF with stirring until a clear viscous solution was obtained. The 2 solutions were then mixed with stirring to homogeneity. The mixture was poured into a glass ring (30-35 mm diameter) resting on a glass plate, and a pad of filter was placed on top of the glass. The solvent was then allowed to evaporate at room temperature over about 2 days. The thickness of the membrane obtained was about 0.5 mm. The size of this membrane was sufficient to prepare about 10 electrodes.

Results and Discussion

The performances of the electrodes prepared with the ion-pair complex atenolol-phosphotungstate as an electroactive material in the membrane were experimentally compared. The results of electrode parameters obtained from the calibration graphs are listed in Table 1.

The low slope values obtained for membranes I and II may be attributed to the plasticizers used, TBP and DBP, respectively, which contained a long alkyl chain attached to the phosphate group, which may decrease the ion exchange process between the electroactive A-TP and the external solution of atenolol, and/or to the steric effect, which decreased the bond strength with the electroactive compound. The potential response of the proposed electrode (IV) at varying concentrations of atenolol gave a slope of 55.91 mV/decade with a detection limit of 5.00 x 10^{-5} M and lifetime of around 90 days (Table 1). However, membrane III gave a slope of 64.07 mV/decade but the lifetime was 7 days. This could be attributed to the incompatibility of NPOE with the complex (A-TP), causing a leaching of the complex from the membrane to the external solution.

A typical calibration curve for the atenolol electrodes is shown in Figures 1 and 2 for membranes I and IV, respectively. The stability of the 4 electrodes was monitored continuously using 1.00 x 10^{-3} M of atenolol solution and evaluated every day. The standard deviation of potential drift obtained for 6 replicated measurements was around 2, 3, 8 and 0.5 mV/day for membranes I, II, III and IV, respectively. This shows that the reproducibility of the potential response for membrane IV was the best.

Table 1. Response characteristics of the atenolol electrodes.

Membrane no.	I	II	III	IV
Plasticizer	DBP	TBP	NPOE	DOPH
Slope mV/decade	34.63	35.16	64.07	55.91
Correlation coefficient (R)	0.9994	0.9988	0.9971	0.9994
Concentration range/M	1.00×10^{-4} – 5.00×10^{-1}	1.00×10^{-4} – 5.00×10^{-2}	1.00×10^{-4} – 1.00×10^{-2}	1.00×10^{-4} – 5.00×10^{-1}
Detection limit	1.10×10^{-5}	1.80×10^{-6}	1.10×10^{-4}	5.00×10^{-5}
Lifetime/day	~ 35	~ 45	~ 7.0	~ 90
Potential drift mV/day	2.0	3.0	8.0	0.5

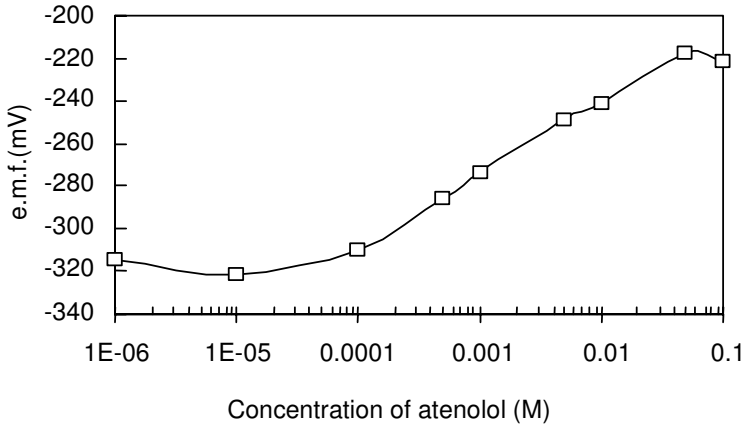

Figure 1. Calibration curve of atenolol selective electrode based on (A-TP) ionophore and DBP plasticizer.

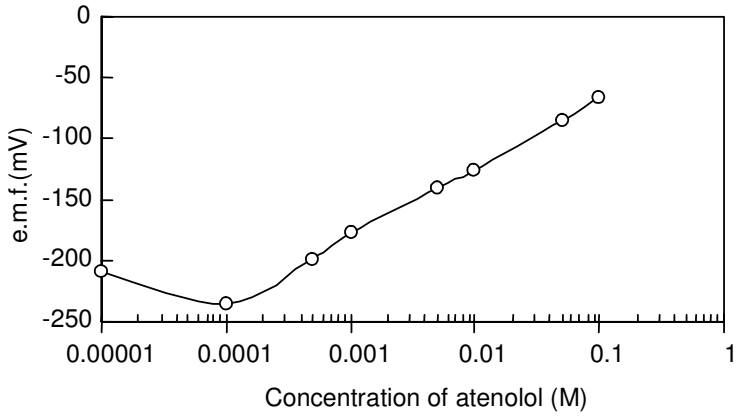

Figure 2. Calibration curve of atenolol selective electrode based on (A-TP) ionophore and DBPH plasticizer.

Effect of pH

The effect of pH on the response of the electrodes was examined by measuring the potential variation over the pH range from 1.0 to 11.5 for 3 different atenolol concentrations, namely 1.00×10^{-4}, 1.00×10^{-3} and 1.00×10^{-2} M. The working pH ranges for the electrodes are listed in Table 2.

Table 2. Working pH ranges for atenolol electrodes at different concentrations of atenolol solutions.

	Detection limit/M		
Membrane no.	1.00 x 10^{-2}	1.00 x 10^{-3}	1.00 x 10^{-4}
I	3.00-9.00	2.00-9.00	4.00-9.00
II	1.00-7.00	2.00-7.50	1.00-9.00
III	3.00-6.00	3.00-6.00	2.00-8.00
IV	3.00-8.00	4.00-9.00	2.00-9.00

A typical plot for the pH effect on atenolol electrodes based on DOPH plasticizer is shown in Figure 3. The pH was adjusted with dilute ammonia and hydrochloric acid solutions.

The observed drifts at higher pH values could be due to the formation of tungsten oxide or ammonium phosphate.

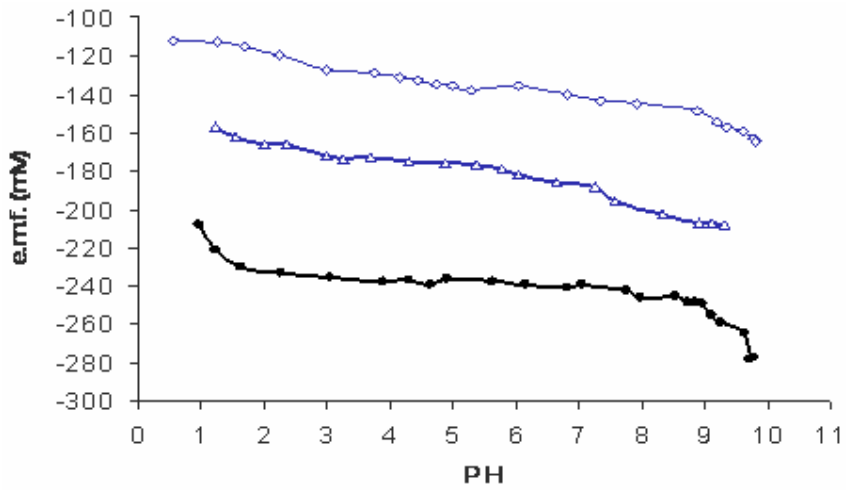

Figure 3. Effect of pH on response of the electrode IV at different atenolol concentrations. o – 10^{-2} M, Δ – 10^{-3} M, •– 10^{-4} M.

Response time

The electrode response time to reach a potential within ±1 mV of the final equilibrium value was determined. The measured response time for the atenolol electrode based on DOPH for 0.01 M atenolol solution was 7.3 and 5.7 s for 1.00 x 10^{-4} M atenolol solution, while for the electrode based on NPOE plasticizer the response time was 7.6 and 5.7 s for 0.01 and 1.00 x 10^{-4}M atenolol solutions, respectively.

Selectivity

A separate solution method was investigated for selectivity coefficient measurement, and was calculated according to the equation: (14,15)

$$\log K_{ate.}^{pot} = [(E_B - E_A) / (2.303\, RT/z_A F)] + (1 - z_A/z_B) \log a_A$$

E_A and E_B, $z_A$and z_B, $a_A$and $a_B$are the potentials, charge numbers and activities for the primary and interfering ions, respectively, and $a_A = a_B = 0.01$ M.

The values of the selectivity coefficient for the electrode based on DOPH and NPOE plasticizers for some monovalent and divalent ions are listed in Table 3.

Table 3. Selectivity coefficient for electrode IV based on DOPH and NPOE plasticizers.

	DOPP			NPOE		
Interfering ion	E_1(mV)	E_2(mV)	Log $K^M_{ate.}$	E_1(mV)	E_2(mV)	Log K^M_{ate}
Na^+	-125	-46	1.4129	-125	-65	0.9365
K^+	-124	-47	1.3771	-124	-63	0.9521
Li^+	-125	-46	1.4129	-125	-70	0.8584
Ba^{2+}	-124	-18	1.9009	-125	-35	1.4097
Mn^{2+}	-126	-18	1.9367	-125	-39	1.3473
Cd^{2+}	-125	-12	2.0261	-126	-30	1.5034

The selectivity coefficients indicate good selectivity for atenolol against alkali, alkaline earth and some common transition metal ions. Moreover, the selectivity coefficient for monovalent ions is lower than that for divalent ions. This may be due to the differences in ionic size, mobility and permeability. The values of log $K^{pot}_{ate.,}$ were found to change from 0.858 to 1.413 for monovalent and from 1.347 to 2.026 for divalent, for both electrodes.

Sample analysis

The concentrations of atenolol in prepared standard solutions were determined using an electrode based on DOPH plasticizer. Four potentiometric techniques were used for the determination of atenolol, namely direct measurement, standard addition (SA), multi-standard addition (MSA) and titration. A standard solution of atenolol with a concentration of 1.00 x 10^{-1} M was used in SA and 1.00 x 10^{-2} M phosphotungstic acid was used as the titrant for titration.

Gran's plots were constructed using Gran's plot paper with 10% volume correction to calculate the equivalence point precisely with MSA and titration.

The results of the quantitative measurements for atenolol solution with relative standard deviation and relative error are listed in Table 4.

Table 4. Samples analysis using atenolol electrode based on DOP plasticizer.

		Concentration calculated by potentiometric methods*			
Atenolol sample	Concentration of atenolol (prepared)/M	Direct measurement	Standard addition	Multi standard	Titration
sample 1	1.028 x 10^{-3}	1.017 x 10^{-3}	1.030 x 10^{-3}	1.034 x 10^{-3}	1.100 x 10^{-3}
sample 2	1.101 x 10^{-3}	1.092 x 10^{-3}	1.050 x 10^{-3}	1.055 x 10^{-3}	1.056 x 10^{-3}
sample 3	1.072 x 10^{-3}	1.037 x 10^{-3}	0.999 x 10^{-3}	1.019 x 10^{-3}	1.002 x 10^{-3}
%RSD		1.01	2.52	1.74	3.64
%RE		0.98	2.46	3.61	4.93

*each value is the average of 3 measurements.

Figure 4 shows the Gran's plot for MSA for the determination of 0.01 M atenolol solution. The calculated %RSD using titration is high (3.64%) compared with the other methods. This may be attributed to the precipitation of A-PT complex on the surface of the membrane and poisoning the electrode.

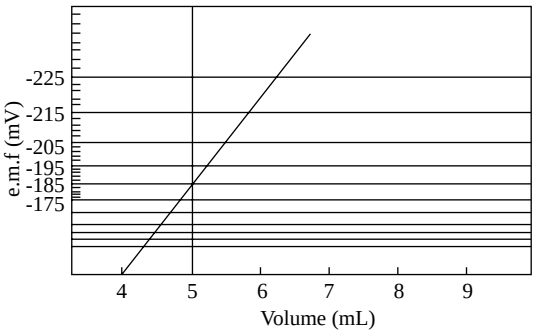

Figure 4. Multi-standard addition method for the determination of 0.01 M atenolol sample using Gran's plot paper with membrane IV.

Figure 5 shows a typical plot for the titration curve of 0.01 M atenolol standard solution with 0.01 M phsophotungstic acid as a titrant using the atenolol electrode based on membrane containing DOPH plasticizer.

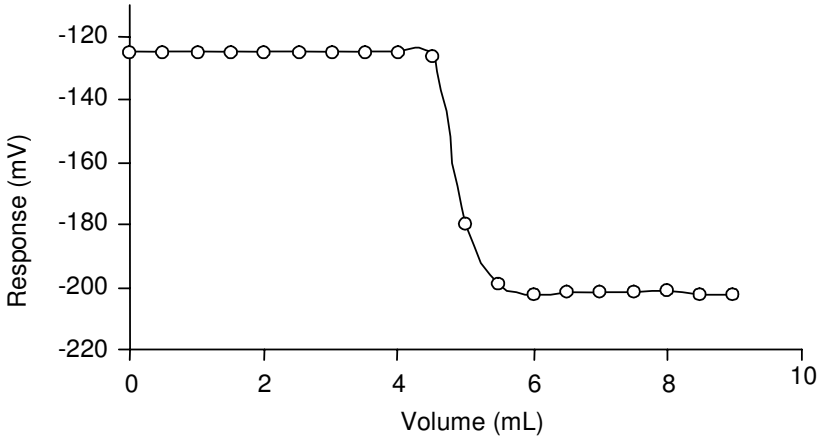

Figure 5. Titration curve for sample solution containing 5 mL of 0.01M atenolol with 0.01 M PT standard solution as titrant.

The direct potentiometric method was applied for the determination of atenolol in pharmaceutical tablets (Tenordin, Ateno and Novaten) as listed in Table 5 using the electrode based on membrane IV. The average recovery for atenolol determination in tablets was around 98.5% with a standard deviation of about $\pm$ 0.1, based on an average of 3 measurements for each sample.

Table 5. Sample analysis for tablets using the atenolol selective electrode based on DOPH plasticizer using the direct potentiometric method.

Pharmaceutical tablets	Tenodin	Ateno	Novaten
Concentration of atenolol (prepared) / M*	1.00×10^{-3}	1.00×10^{-3}	1.00×10^{-3}
Concentration of atenolol (found) / M	0.9854×10^{-3}	0.9834×10^{-3}	0.9850×10^{-3}
%recovery	98.54	98.34	98.50
%error	1.46	1.66	1.50

*Prepared based on nominal amount of atenolol given by the manufacturer's leaflet.

Conclusion

In this paper, we have described a potentiometric method for atenolol determination in pharmaceutical drugs using an ion-selective electrode. The best electrode obtained in this study was based on a membrane containing atenolol-phosphotungstate complex and di-octyl phthalate as a plasticizer. The average recovery for atenolol determination in pharmaceutical tablets was around 98.5% with a standard deviation of ± 0.1. The advantage of the method is its simplicity and selectivity in measuring atenolol over wide pH and atenolol concentration ranges without any major interference from mono- or divalent metal ions.

References

1. The pharmaceutical codex, "**Principle and Practical of Pharmaceutics**" 21^{st} ed., The Pharmaceutical Press, London (1994).
2. A.S. Alwan and Y.Z. Abou, "**Iraqi Drugs Guide**" 1^{st} ed., Iraq (1990).
3. Y.G. Yee, P. Rubin and T.F. Blaschke, **J. Chromatogr. A 171**, 357-362 (1979).
4. I. Rapado-Martinez, M.C. Garcia-Alvarez-Coque and R.M. Villanueva-Camonas, **Analyst 121**, 1677-1682 (1996).
5. M. Sundaresan, S. Patil, I.C. Bhoir and Y.P. Patel, **J. Chromatogr. A 828**, 283-286 (1998).
6. A.P. Argekar and J.G. Sawant, **J. Liq. Chromatogr. 12**, 202-206 (1999).
7. P. Umapathi, **Int. J. Pharm. 108**, 11-19 (1994).
8. R.I. Stefan, G.E. Baiulescu and H.Y. Aboul-Enein, **Trends Anal. Chem. 27**, 307 (1997).
9. H.Y. Aboul-Enein and X.X. Sun, **Analusis 28**, 855-858 (2000).
10. H.Y. Aboul-Enien, X.X. Sun and C.J. Sun, **Sensor 2**, 424-431 (2002).
11. N. Alizadeh and R. Mehdipour, **J. Pharmaceut. Biomed. 30**, 725-731 (2002).
12. G.J. Moody, R.B. Oke and J.D.R. Thomas, **Analyst 95**, 910-918 (1970).
13. J.E.W. Davis, G.J. Moody, W.M. Price and J.D.R. Thomas, **Lab. Practice. 22**, 20 (1973).
14. Y. Umezawa, K. Umezawa and H. Sato, **Pure Appl. Chem. 67**, 507-518 (1995).
15. Y. Umezawa, P. Buhlmann, K. Umezawa, K. Tohda and S. Amemiya, **Pure and Appl. Chem. 72**, 1851-2082 (2000).