

RESEARCH ARTICLE

New Poly Vinyl Chloride Ion Selective Electrode for Potentiometric Analysis of Propranolol in its Pharmaceutical Formulations and Human Fluids

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ABSTRACT

New, simple, sensitive and rapid method for the determination of propranolol in the pharmaceutical preparations and human fluids. The Buildup and electrochemical response characteristics of a poly vinyl chloride (PVC) selective membrane electrode for the determination of propranolol (POP) are described in this research. The proposed electrodes was composed of propranolol-bromophenol blue as ion-exchanger and Di-butyl phthalate (DBPH) (electrode A), tris (2-ethylhexyl) phosphate (TEHP) (electrode B), and ortho-nitrophenyloctylether (ONPOE) (electrode C), as plasticizers. The slope was 50.94, 57.77, and 49.75 mV/decade for electrode A, B and C. the linear range was $5 \times 10^{-5} - 1 \times 10^{-2}$, $1 \times 10^{-4} - 1 \times 10^{-2}$, and $5 \times 10^{-5} - 1 \times 10^{-2}$ M, a detection limit of 4.2×10^{-5} , 8.9×10^{-5} , and 4.8×10^{-5} M, lifetime of 21, 42, and 1-day, respectively. Electrode B gives the best results, so the application of pharmaceutical and human fluids was based upon this electrode, the recovery percentage was 103, 101, 102.5, and 104 for POP tablet 10mg, tablet 40mg, urine and plasma by standard addition method, respectively.

Keywords: Ion-selective electrode, Propranolol hydrochloric acid, Sensors.

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INTRODUCTION

POP is a beta-blocker medication (Figure 1), which is a white solid material; its chemical formula is $C_{16}H_{21}NO_2$ with a molecular weight of 259.34 g/mol. Beta-blocker have an influence on the heart and circulation. Propranolol is used to treat high blood pressure, tremors, heart rhythm disorders; it prevents migraines and heart attack. Because of the propranolol's therapeutic and pharmacological relevance, it has been determined in pharmaceutical preparations through various techniques, such as spectrophotometry,^{1,2} chromatography,³⁻⁵ spectrofluorimetry,⁶⁻⁹ and chemiluminescence.^{10,11}

For the pharmaceutical analysis, an alternative technique is presented by potentiometry through utilizing the ion-selective electrode (ISE) (Figure 2), which is characterized by simplicity, rapidity of analysis, low cost, and low detection limit.

This work aimed to provide a liquid membrane electrode that is based on the dissolution of an ionophore in the plasticizer, which is low permeable, with the addition of PVC, which is working as supporting material.

The proposed electrode was positioned between two phases of aqueous solutions, the outer one was the sample solution, and the other one was the inner reference solution, which has a fixed concentration of analyte ion. One was the inner reference solution, which has a fixed concentration of analyte ion. The

potential difference was measured across the membrane of the electrode by using two reference electrodes placed in the aqueous phase.

The prepared electrode was used for the determination of POP in the pharmaceutical dosage form and human fluids.

EXPERIMENTAL

Apparatus

An expandable ion analyzer (model-EA940 Orion Research) was used for the electrochemical measurements in conjunction with Metrohm AG 9100 herisau reference electrode. A pH meter of (model-BP3001 pH professional benchtop meter) was used to check the pH of the solutions.

The assembly of the electrochemical cell was as follows:
Ag/AgCl | Internal solution (0.01 M) of POP | PVC membrane | Sample solution | KCl (sat'd).

Using SHIMADZU Fourier transform infrared (FTIR) spectro-photometer (model-8300).

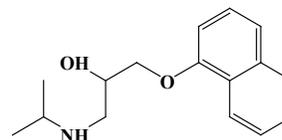


Figure 1: Chemical structure of POP

Materials and Reagents

All the chemical used in this work was of analytical or pharmacopeia grade. Distilled water was used in the preparation of the solvents. Propranolol hydrochloride POP was obtained from Bromophenol blue (BPB) was obtained from Fluka. DBPH supplied by Ferak. TEHP, ONPOE was obtained from polyvinyl chloride (PVC) and tetrahydrofuran (THF) was supplied by Fluka.

Stock solution of 0.01 M (LiCl, KCl, NaCl, MgCl₂, CaCl₂, ZnCl₂, AlCl₃, FeCl₃, and CrCl₃) was prepared. Other diluted solutions were prepared by the subsequent dilution of the stock solutions.

Preparation of Ionophore

The preparation of propranolol ion-selective electrode based on the use of propranolol-bromophenol blue (POP-BPB) as an electroactive substance.

The preparation of POP-BPB ion-pair was performed by mixing 100 mL of 0.01 M solution of POP with 100 mL of 0.01 M BPB with stirring. Then, the precipitate was filtered, washed with distilled water, and then dried for one-day. The ion-pair-composition was curtailed by using FTIR.

Preparation of Membrane

The solidification method of propranolol into the PVC matrix membrane was made as described by Davis *et al.*¹²

Add 0.040 gram of the ion-pair matrix, 0.360 gram of

plasticizer, 0.17 gram of PVC powder, and then add 7 mL of THF with stirring, until the formation of a viscous solution.

This solution was poured into a glass molding ring of about 30 mm length and 35 mm diameter, consists of two pieces: one of them is the cylinder, and the other is the plate. These two pieces was glued together by using PVC-THF viscous mixture.

The upper side of the cylinder was covered with filter paper, a heavyweight ~200g was placed. This assembly was left for 2-3 days to ensure the evaporation of the solvent.

Calibration Curve

The prepared electrode was calibrated by the transferring of an appropriate amount of the aqueous POP solution $1 \times 10^{-6} - 1 \times 10^{-2}$ M, followed by immersing the POP membrane electrode together with the reference electrode in the same solution; readings recorded after the stabilization of the potentials. The calibration curve was constructed between potentials and the logarithm of the POP concentrations.

Selectivity

Two methods were used to determine the selectivity coefficient of the potentiometric electrodes toward various species, which are the separate solution method (SSM) and match potential method (MPM).¹³

In the SSM method, the following equation was used:

$$K_{A,B}^{\text{pot}} = a_A^{(1 - z_A/z_B)} e^{(E_B - E_A) z_A F / (R T)}$$

Where EA is the potential of the drug and EB for the interfering ions.

While in the MPM method, the following equation were used:

$$K_{A,B}^{\text{pot}} = (a_A' - a_A) / a_B$$

Sample Preparation

Propranolol hydrochloride was determined in the formulation of tablets. Its concentration was ranging from 1.0×10^{-6} to 1.0×10^{-2} M. The POP was determined by direct method and standard addition method. A total of 10 tablets of POP were powdered and mixed to get the average value of tablet's weight. 0.0012 grams of POP was accurately weighted and dissolved in 50 mL volumetric flask. This procedure gives 10^{-4} M solution of POP. These solutions were analyzed by the above methods using the present electrode. Each analysis was repeated three times (Figure 3).

Sample Analysis

The direct method in which the sample of various concentrations

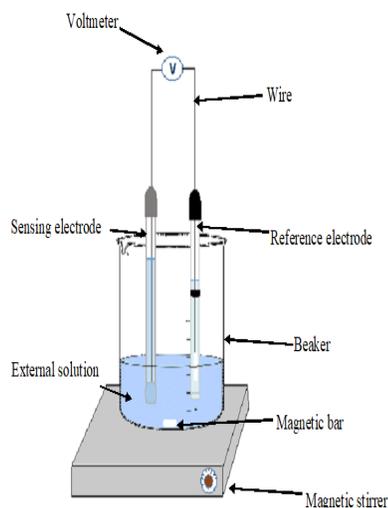


Figure 2: Schematic diagram of the ISE cell



Figure 3: Manufactured membranes of POP using several plasticizers

1.0×10^{-6} to 1.0×10^{-2} M was applied, and the potential was recorded in order to create the calibration curve.

The standard addition method in which 0.1 mL of 1×10^{-2} M POP were added to 10 mL of a sample of various concentrations 1×10^{-4} M has applied the potential after each increment was recorded, and used to calculate the concentration of POP in a drug sample.

Determination of POP in Human Fluids

2.5 mL of serum and urine were taken from a healthy person 0.25 mL from (1×10^{-2}) M POP standard solution were added to 25 mL volumetric flask, and completed to the mark with distilled water, and then subjected to the potentiometric analysis.

RESULTS AND DISCUSSION

Influence of Plasticizers

The effect of the plasticizers on the POP electrode's response was studied by using three plasticizers which were: DBPH, TEHP, and ONPOE (Figures 4 and 5).

Plasticizers was added to dissolve the ion-pair complex and to set the permittivity of the membrane, and the mobility of the ion-exchanger in order to give the prepared electrode, the best selectivity, and sensitivity.

Influence of pH

Effect of pH on the electrode's potential was evaluated by measuring the potential of the cell at the concentrated of (1×10^{-4} and 1×10^{-3}) M of POP solution. The adjustment of the pH was

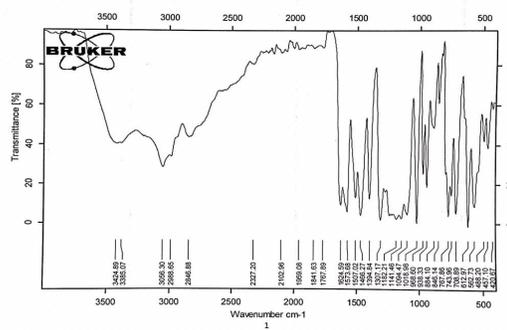


Figure 5: FTIR spectrum of POP-BPB ion pair

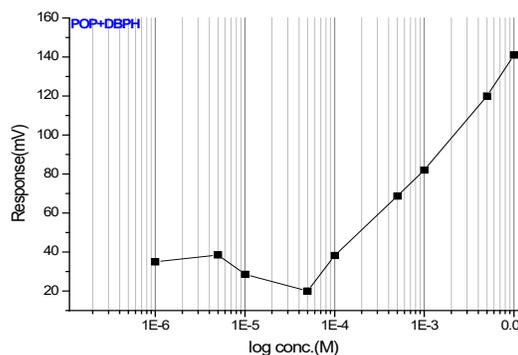


Figure 6: Calibration of POP-DBPH

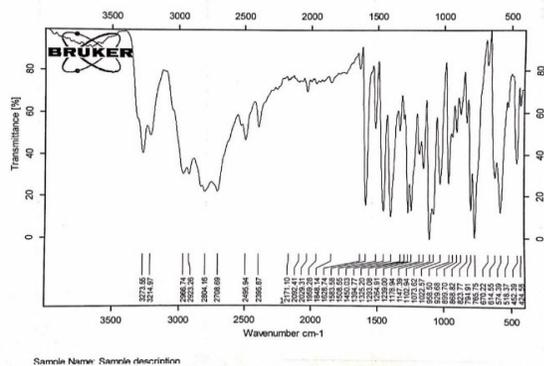


Figure 4: FTIR spectrum of POP pure drug

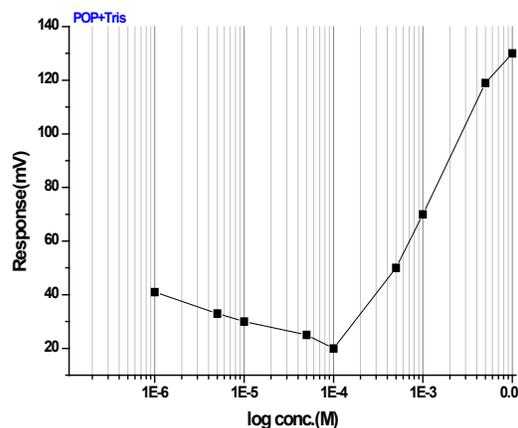


Figure 7: Calibration of POP-TEHP

Table 1: Effect of plasticizers on the parameters of POP electrode

Parameters	DBPH	TEHP	ONPOE
Slope (mV/decade)	50.94	57.77	49.75
Detection limit (M)	5×10^{-5}	1×10^{-4}	5×10^{-5}
Linear range (M)	$5 \times 10^{-5} - 1 \times 10^{-2}$	$1 \times 10^{-4} - 1 \times 10^{-2}$	$5 \times 10^{-5} - 1 \times 10^{-2}$
Response time (sec)	60	60	
Life time (day)	45	52	3
pH	4-8	4-8	4-8
R	0.9977	0.9944	0.9981

made by the addition of some drops of 0.1 M hydrochloric acid or sodium hydroxide (Figures 6 and 7) Table 1.

From Figures 8 to 10, it can notice that POP electrodes do not respond to pH changes in the range 4 to 8.

Response Time and Lifetime

The response time of the electrode can be defined as the time required for the electrode to reach a stable potential after

immersing the proposed electrode and the reference electrode in 1×10^{-6} and 1×10^{-2} M of POP solution (Figures 11-13).

The lifetime of the electrode was measured by employing the electrode for 6 weeks period time. After this time the slope tends to be decreasing, and the detection limit tends to be increasing, and calibration curve plotted with the series of standard solutions $1 \times 10^{-6} - 1 \times 10^{-2}$ M of POP solution.

Selectivity

The interferences of some inorganic cations such as: Li^+ , Na^+ , K^+ , Mg^{2+} , Ca^{2+} , Zn^{2+} , Al^{3+} , Cr^{3+} and Fe^{3+} was studied

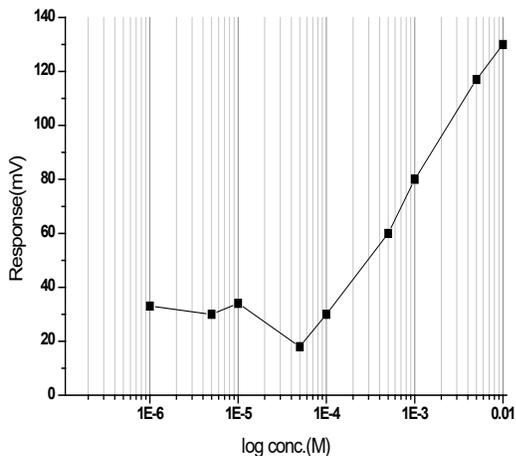


Figure 8: Calibration of POP-ONPOE

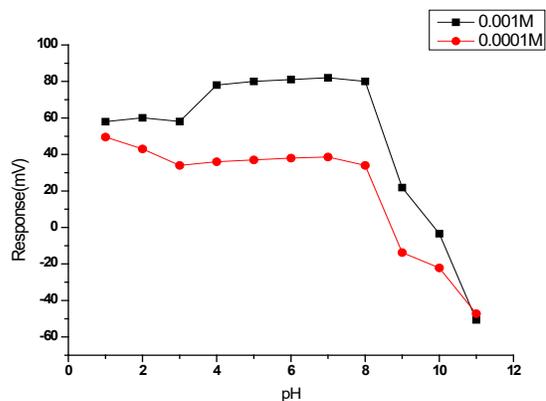


Figure 9: Effect of pH for POP-DBPH

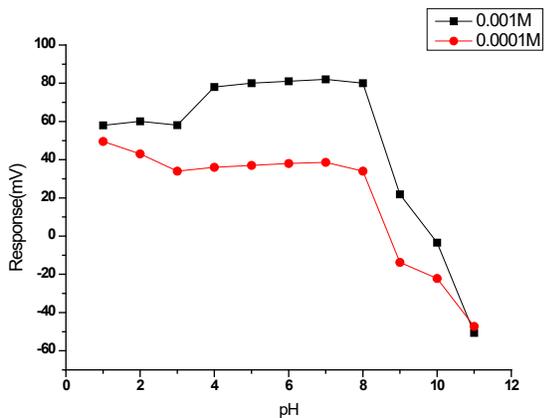


Figure 10: Effect pH of POP-TEHP

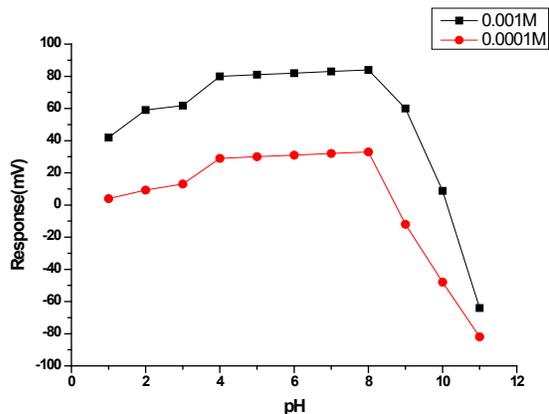


Figure 11: Effect of pH POP-ONPOE

Table 2: Selectivity coefficient of POP-TEHP

Conc. mol.L ⁻¹	$K_{A,B}$								
	Li^+	Na^+	K^+	Ca^{+2}	Mg^{+2}	Zn^{+2}	Cr^{+3}	Fe^{+3}	Al^{+3}
1.0×10^{-2}	9.02×10^{-3}	7.19×10^{-3}	6.51×10^{-3}	4.21×10^{-4}	4.08×10^{-4}	6.02×10^{-4}	1.34×10^{-4}	2.21×10^{-4}	1.88×10^{-4}
5.0×10^{-3}	1.54×10^{-2}	1.13×10^{-2}	1.02×10^{-2}	4.77×10^{-4}	4.37×10^{-4}	6.61×10^{-4}	1.24×10^{-4}	2.07×10^{-4}	1.88×10^{-4}
1.0×10^{-3}	9.83×10^{-2}	8.08×10^{-2}	7.55×10^{-2}	1.44×10^{-3}	1.38×10^{-3}	1.72×10^{-3}	3.10×10^{-4}	4.29×10^{-4}	4.30×10^{-4}
5.0×10^{-4}	2.08×10^{-1}	1.80×10^{-1}	1.74×10^{-1}	2.19×10^{-3}	2.10×10^{-3}	2.59×10^{-3}	4.29×10^{-4}	5.95×10^{-4}	6.02×10^{-4}
1.0×10^{-4}	7.35×10^{-1}	6.22×10^{-1}	5.41×10^{-1}	3.23×10^{-3}	3.14×10^{-3}	5.05×10^{-3}	4.87×10^{-4}	6.56×10^{-4}	7.31×10^{-4}
5.0×10^{-5}	4.68×10^{-1}	3.70×10^{-1}	2.67×10^{-1}	1.33×10^{-3}	1.21×10^{-3}	2.10×10^{-3}	1.82×10^{-4}	2.03×10^{-4}	2.43×10^{-4}
1.0×10^{-5}	5.34×10^{-1}	4.86×10^{-1}	3.72×10^{-1}	6.57×10^{-4}	6.95×10^{-4}	1.15×10^{-3}	7.39×10^{-5}	7.84×10^{-5}	1.02×10^{-4}
5.0×10^{-6}	4.31×10^{-1}	4.61×10^{-1}	3.02×10^{-1}	4.09×10^{-4}	4.19×10^{-4}	6.69×10^{-4}	3.84×10^{-5}	4.56×10^{-5}	5.59×10^{-5}
1.0×10^{-6}	3.96×10^{-1}	3.81×10^{-1}	2.31×10^{-1}	1.32×10^{-4}	1.53×10^{-4}	2.37×10^{-4}	9.71×10^{-6}	1.14×10^{-5}	1.39×10^{-5}

using separate solution method and match potential method. The selectivity coefficient values was tabulated in the Table 2 and Figures 14-17).

Analytical Application

The proposed electrode was utilized successfully for the determination of POP in the standard drug, pharmaceutical

preparations (tablets), and human fluids (plasma and urine) by direct method and standard addition method; the results were shown in Tables 3 and 4.

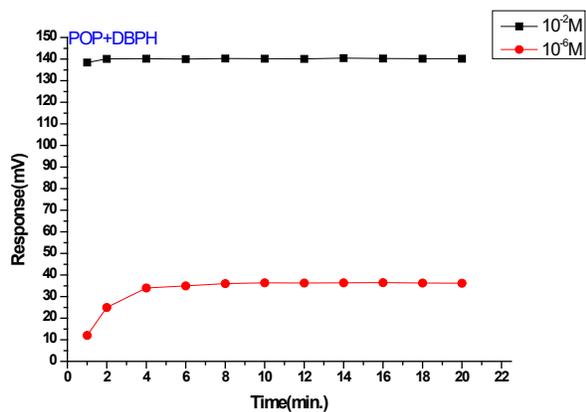


Figure 12: Response time of POP-DBPH

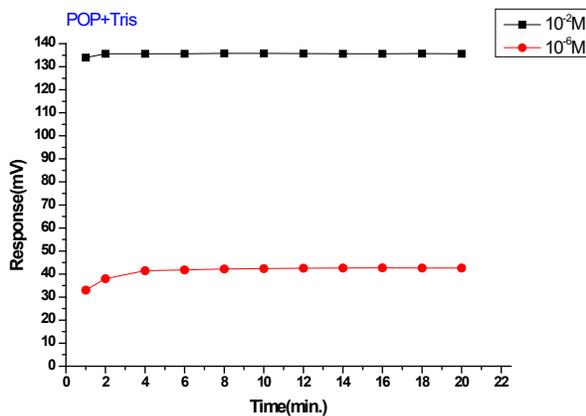


Figure 13: Response time of POP-TEHP electrode

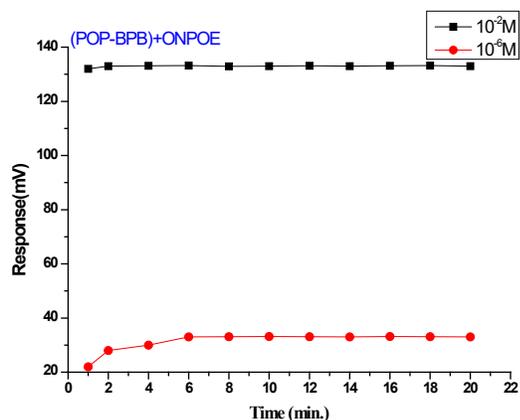


Figure 14: Response time of POP-ONPOE

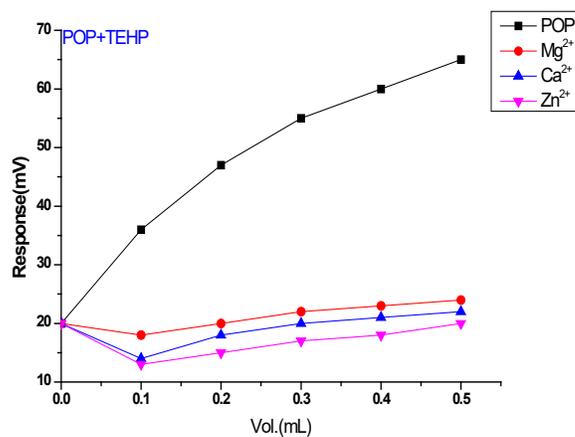


Figure 16: Selectivity for POP-TEHP for di-cations by match potential method

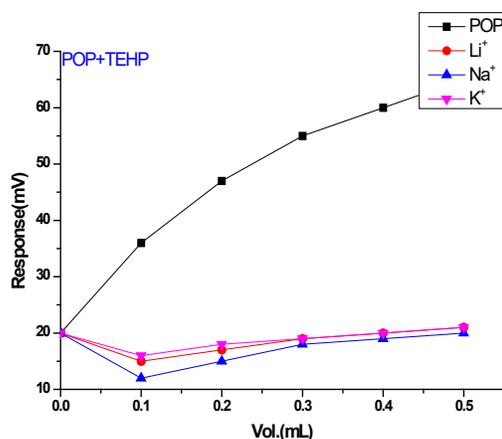


Figure 15: Selectivity for POP-TEHP for mono-cations by match potential method

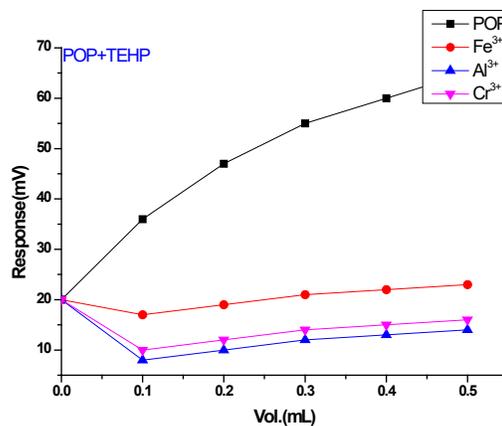


Figure 17: Selectivity for POP-TEHP for tri-cations by match potential method

Table 3: Estimation of the pharmaceutical application and human fluids by the standard addition method

Drug	Original conc. (M)	RSD% n = 3	Found conc. (M)	RE%	RC%
Standard of propranolol	1×10^{-4}	2.45	1.01×10^{-4}	1.7	101.7
Propranolol (tablets 10 mg)	1×10^{-4}	0.24	1.03×10^{-4}	3	103
Propranolol (tablets 40 mg)	1×10^{-4}	2.11	1.01×10^{-4}	1	101
Urine	1×10^{-4}	0.64	1.02×10^{-4}	2.5	102.5
Plasma	1×10^{-4}	1.29	1.04×10^{-4}	4	104

Table 4: Volume at intercept with X axis and calculation the concentration C_U (M) for electrode B by MSA method

Drug	Conc. (M)	C_U (M)	RE%	RC%
Standard of propranolol	1×10^{-4}	0.99×10^{-4}	-1	99
Propranolol (tablets 10mg)	1×10^{-4}	0.99×10^{-4}	-1	99
Propranolol (tablets 40mg)	1×10^{-4}	0.98×10^{-4}	-2	98
Urine	1×10^{-4}	0.9×10^{-4}	-10	90
plasma	1×10^{-4}	1.01×10^{-4}	1	101

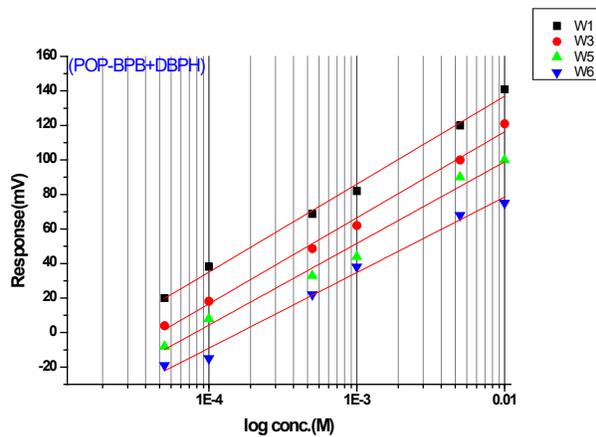


Figure 18: Lifetime of POP-DBPH.

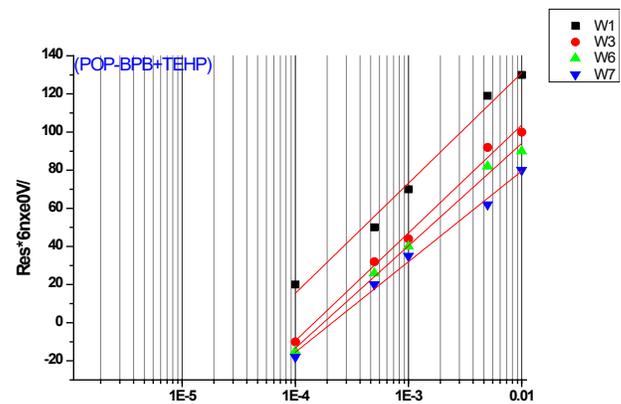


Figure 19: Lifetime of POP-TEHP

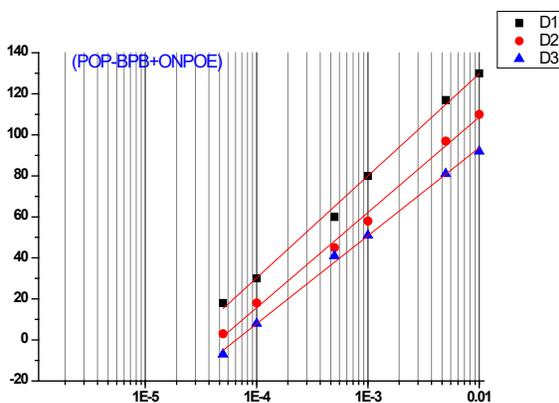


Figure 20: Lifetime of POP-ONPOE

The direct method was the simplest method that used for gaining the quantitative results using ISE.¹⁶

The calibration curve was plotted, then the concentrated of POP in tablets were calculated by using the linear equation of the calibration curve (Figures 18-20).

In the standard addition method, the concentrated of POP was determined by adding 0.1 mL of 1×10^{-2} M POP were added to 10 mL of 1×10^{-4} M. The change in potentials readings was recorded after each addition by the following equation¹⁷:

$$C_x = C_s V_s / [(V_x + V_s) \times 10^{\Delta E/s} - V_x]$$

C_x and V_x was the concentrated and volume of unknown sample respectively. C_s and V_s was the concentrated and volume of standard solution, respectively. S was the slope value of the calibration curve, and ΔE was the change in the potential of the electrode.

CONCLUSION

In this study, the construction of new three electrodes of POP was based on a plasticized PVC membrane containing the ion-exchanger that formed between POP and BPB. It was a sensitive, precise, rapid, and inexpensive method that was used in the determination of POP in the pure form, pharmaceutical preparations, and human fluids.

The electrode B has shown good performance with the time stability up to 7 weeks.

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