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New PVC 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 (POP) in the pharmaceutical preparations and human fluids. The Buildup and electrochemical response characteristics of a poly (vinyl chloride) (PVC) membrane selective electrode for the determination of (POP) was described in this research. The proposed electrodes were composed of Propranolol-Bromophenol blue (POP-BPB) as ion-exchanger and Di-butylphthalate (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 (5×10^{-5} - 1×10^{-2}), (1×10^{-4}-1×10^{-2}) and (5×10^{-5} - 1×10^{-2}) M, detection limit of (4.2×10^{-5}), (8.9×10^{-5}) and (4.8×10^{-5}) M, life time of (21), (42) and (1) days, respectively. Electrode B give the best results, so the application of pharmaceutical and human fluids was based upon this electrode, the recovery% was (103), (101), (102.5) and (104) % for POP tablet 10mg, tablet 40mg, urine and plasma by standard addition method respectively.

Keywords: Propranolol hydrochloric acid, Sensors, Ion selective electrode

INTRODUCTION

Propranolol (POP) is a beta-blocker medication. It selectively blocks 1 receptor in the heart which decreases the force of contraction and heart rate, then leads to decreased blood pressure. It is a white solid material, and the chemical formula is $C_{16}H_{21}NO_2$ with molecular weight of 259.34 g/mol. Beta-blocker has an influence on the heart and circulation. Propranolol is used to treat high blood pressure, tremors, heart rhythm disorders, and prevents migraines and heart attacks. Due to 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) which is characterized by simplicity, rapidity of analysis, low coast and low detection limit. The aim of this work is to provide liquid membrane electrode that is based on the dissolution of ionophore in the plasticizer which is low permeable, with the addition of poly (vinyl chloride) PVC which works as a 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 analytic ion. The potential difference was measured across the membrane of the electrode by using two reference electrodes that were placed in aqueous phase. The prepared electrode was used to determine the POP in the pharmaceutical dosage form and human fluids. The ion-pair complex formation of Propranolol is explained in **Figure 1**.

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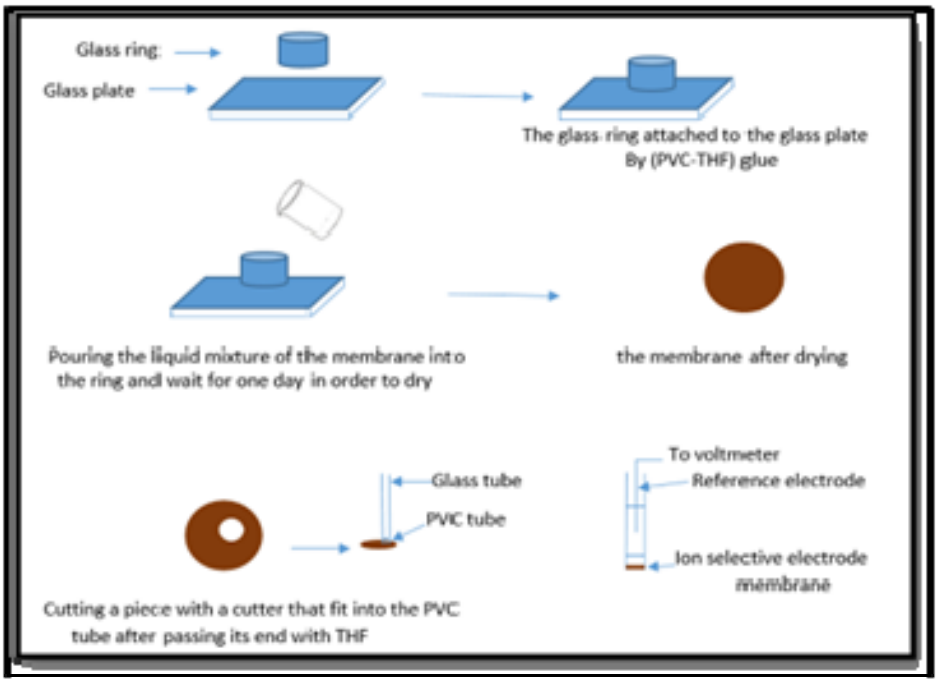

Figure 1. Assembling the Ion Selective Electrode.

RESULT AND DISCUSSION

New membranes were prepared for the determination of POP in the pharmaceutical preparations and human fluids, the characterization of these electrodes based on the ion-pair using different plasticizers were described. The new complex (POP-BPB) was proved by the FTIR spectrum as shown in **Figures 2 & 3.**

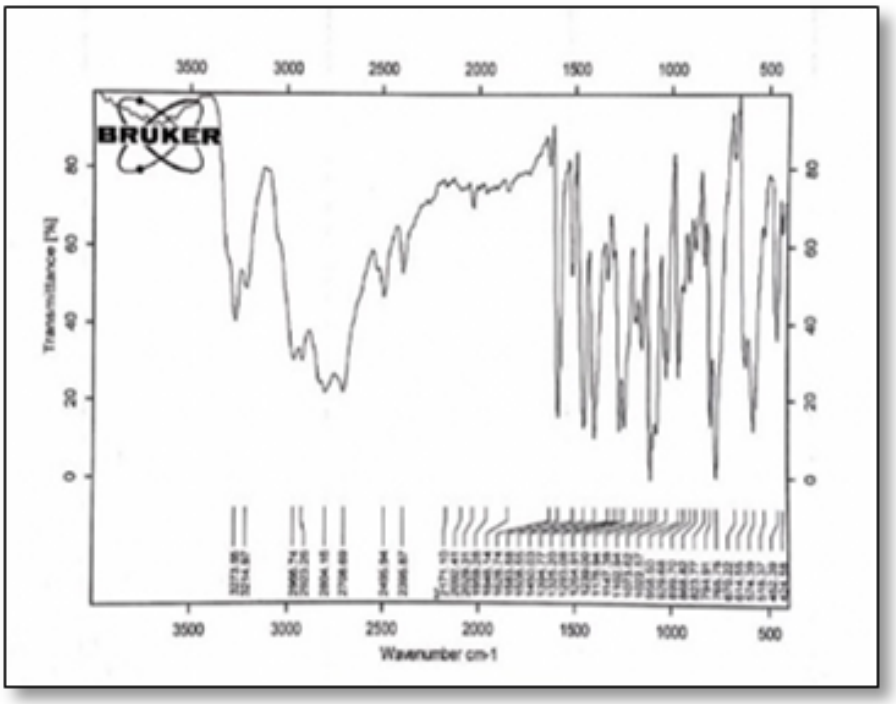

Figure 2. FTIR Spectrum of POP Pure Drug.

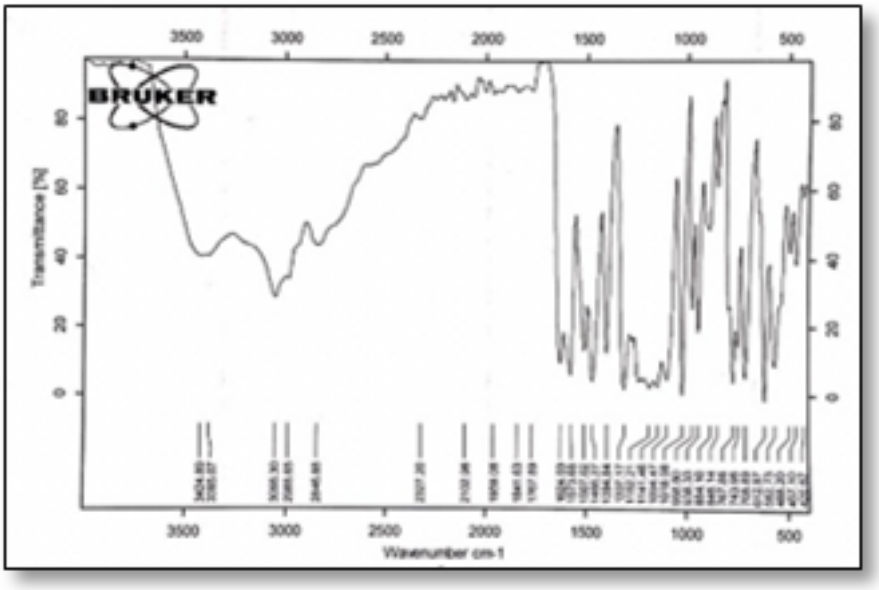

Figure 3. FTIR spectrum of POP-BPB ion pair.

Influence of plasticizers

The effect of the plasticizers on the POP electrode's response was studied by using three plasticizers which are: Di-butylphthalate (DBPH), Tris (2-ethylhexyl) phosphate (TEHP) and Ortho-nitro phenyl- octylether (ONPOE).

Plasticizers were 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 [12].

First electrode for POP drug

This electrode consisted of (POP-BPB) as ion pair, DBPH as plasticizer and PVC as supported which dissolved in THF solvent. The calibration curve for the first electrode was plotted between concentrations range (1×10^{-6}-1×10^{-2}) M of POP drug and the measured potential for each concentration. The statistical treatments of the measured potential are listed in **Table 1.**

Table 1. Response of (POP-BPB) First Electrode.

POP concentration (M)	Average response (mv)	RSD%; n=3
1.0×10^{-2}	141	1.219
5.0×10^{-3}	120	1.502
1.0×10^{-3}	82	1.468
5.0×10^{-4}	68.7	1.005
1.0×10^{-4}	38.2	0.184
5.0×10^{-5}	20	1.828
1.0×10^{-5}	28.6	0.759
5.0×10^{-6}	38.5	0.176
1.0×10^{-6}	35	1.061

Second electrode for POP drug

The second electrode was prepared from (POP-BPB) as ion pair, TEHP as plasticizer and PVC as supported which dissolved in THF solvent. The calibration curve for the second electrode was plotted between concentrations range (1×10^{-6}-1×10^{-2}) M of POP drug and the measured potential for each concentration. The statistical treatments of the measured potential are listed in **Table 2.**

Table 2. Response of (POP-BPB) Second Electrode.

POP concentration (M)	Average response (mv)	RSD%; n=3
1.0×10^{-2}	130	0.656
5.0×10^{-3}	119	0.406
1.0×10^{-3}	70	0.321
5.0×10^{-4}	50	0.251
1.0×10^{-4}	20	0.718
5.0×10^{-5}	25	0.502
1.0×10^{-5}	30	0.157
5.0×10^{-6}	33	0.311
1.0×10^{-6}	41	0.128

Third Electrode for POP Drug

This electrode was synthesized from (POP-BPB) as ion pair, ONPOE as plasticizer and PVC as supported which dissolved in THF solvent. The calibration curve for the third electrode was plotted between concentrations range (1×10^{-6} - 1×10^{-2}) M of POP drug and the measured potential for each concentration. The statistical treatments of the measured potential are tabulated in **Table 3**.

Table 3. Response of (POP-BPB) third electrode.

POP concentration (M)	Average response (mv)	RSD%; n=3
1.0×10^{-2}	130	1.793
5.0×10^{-3}	117	1.831
1.0×10^{-3}	80	1.637
5.0×10^{-4}	60	1.064
1.0×10^{-4}	30	2.181
5.0×10^{-5}	18	1.092
1.0×10^{-5}	34	1.288
5.0×10^{-6}	30	1.727
1.0×10^{-6}	33	0.720

Influence of pH

The effect of pH on the electrode's potential was evaluated by measuring the potential of the cell at the conc. of (1×10^{-4} and 1×10^{-3}) M of POP solution. The adjustment of the pH was made by adding some drops of (0.1) M hydrochloric acid or sodium hydroxide. At the low pH level, the potential of the electrodes increased, this is because the electrode has responded to the H^+ ions. While at high pH levels, the potential of the electrodes dropped sharply because of the poisoning of the membrane by the formation of the white precipitation. From **Figures 4-6** it can be noticed that POP electrodes do not respond to pH changes in the range [4-8].

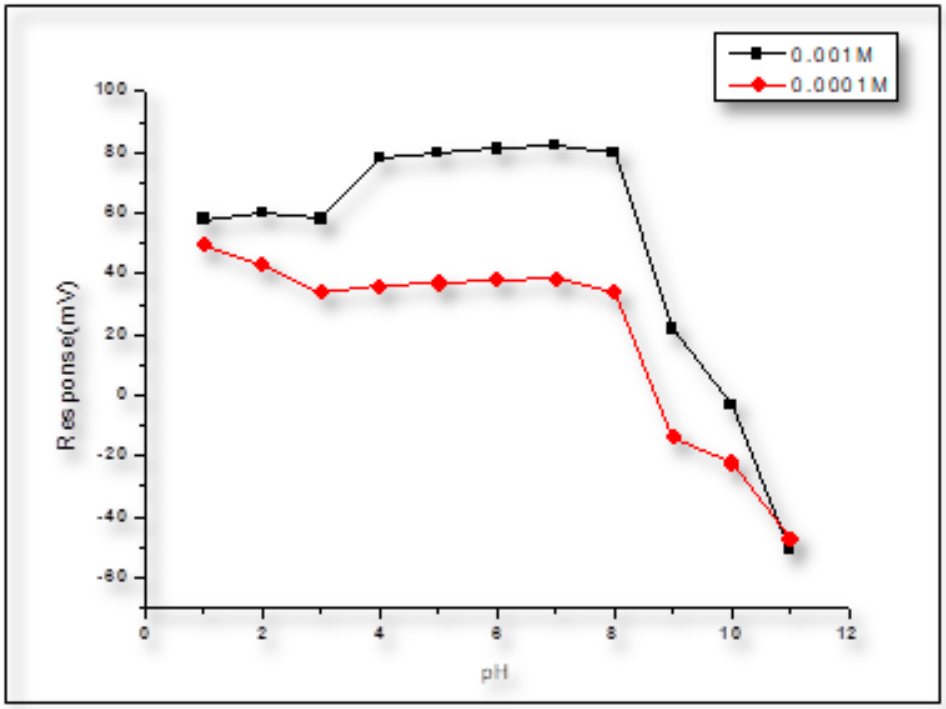

Figure 4. Effect of pH for Electrode A.

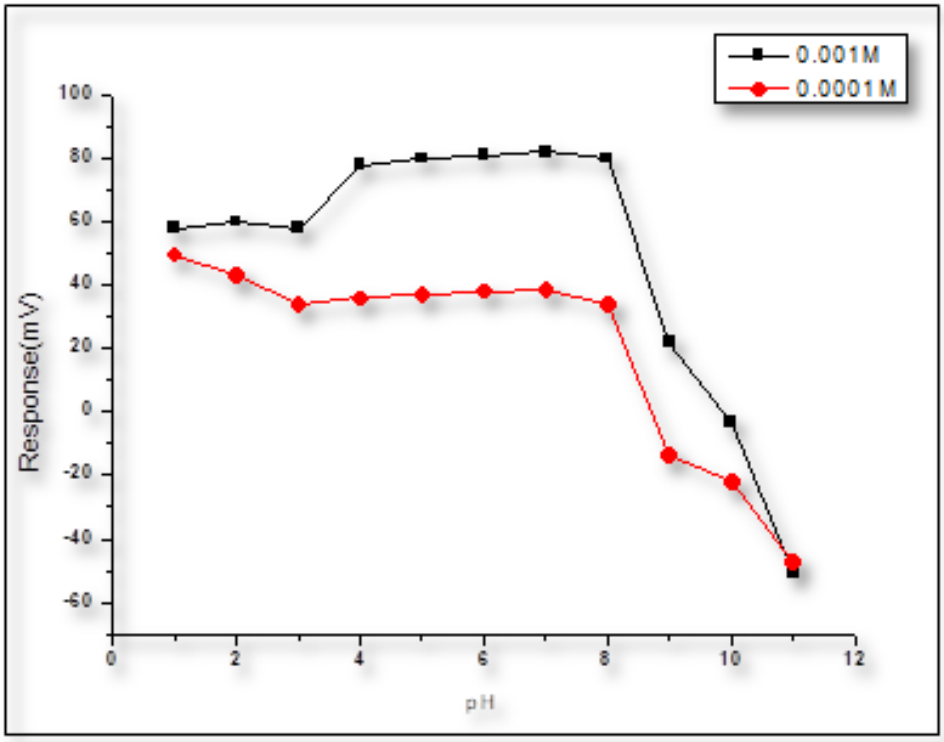

Figure 5. Effect of pH for electrode B.

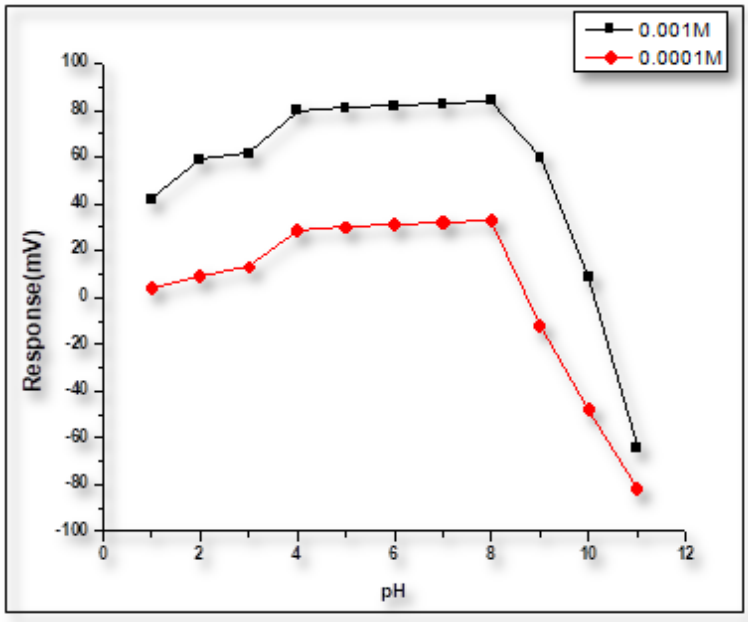

Figure 6. Effect of pH for Electrode C.

Response time and life time

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. The proposed electrodes gave steady potentials after (1), (0.8) and (0.9) min at (1×10^{-2}) M and after (3), (3.8) and (4.5) min at (1×10^{-6}) M for electrode A, B and C respectively. The lifetime of the three electrodes was measured and it was (21), (42) and (1) day for electrode A, B and C respectively. After this time the slope tends to be decreased and the detection limit tends to be increased because of the leaching of the ion pair from the membrane to the external solution **(Table 4)**.

Table 4. 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)	4.2×10^{-5}	8.9×10^{-5}	4.8×10^{-5}
Linear range (M)	5×10^{-5} - 1×10^{-2}	1×10^{-4}- 1×10^{-2}	5×10^{-5} - 1×10^{-2}
Response time (min.)	1.0 at 10^{-2}	0.8 at 10^{-2}	0.9 at 10^{-2}
	3.0 at 10^{-6}	3.8 at10^{-6}	4.5 at10^{-6}
Life time (day)	21	42	1
pH	4-8	4-8	4-8
R	0.9977	0.9944	0.9981

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) were studied using the separate solution method (SSM) and the Match potential method (MPM). The selectivity coefficient values by (SSM) were calculated by Nickolsky-Eisenman equation and tabulated in **Table 5**.

Table 5. Selectivity coefficient of electrode B.

Conc. M	$K_{A,B}$								
	Li^{+}	Na^{+}	K^{+}	Ca^{+2}	Mg^{+2}	Zn^{+2}	Cr^{+3}	Fe^{+3}	Al^{+3}
1.0×10-2	4.05×10^{-1}	2.42×10^{-2}	1.56×10^{-3}	8.85×10^{-5}	1.78×10^{-4}	1.00×10^{-3}	1.89×10^{-3}	6.48×10^{-4}	1.91×10^{-3}
5.0×10^{-3}	9.57×10^{-2}	3.18×10^{-2}	3.11×10^{-3}	1.43×10^{-4}	2.64×10^{-4}	1.23×10^{-3}	2.62×10^{-3}	1.08×10^{-3}	2.73×10^{-3}
1.0×10^{-3}	8.85×10^{-2}	8.81×10^{-2}	2.09×10^{-2}	3.34×10^{-4}	3.71×10^{-4}	1.22×10^{-3}	1.14×10^{-3}	1.49×10^{-3}	1.24×10^{-3}
5.0×10^{-4}	1.71×10^{-1}	7.84×10^{-1}	3.57×10^{-2}	3.49×10^{-4}	5.36×10^{-4}	7.52×10^{-4}	6.72×10^{-4}	3.29×10^{-3}	1.29×10^{-3}
1.0×10^{-4}	1.23×10^{-1}	1.30×10^{-1}	3.35×10^{-1}	1.45×10^{-3}	2.01×10^{-3}	8.44×10^{-3}	5.66×10^{-4}	2.33×10^{-3}	1.57×10^{-4}
5.0×10^{-5}	3.68×10^{-1}	3.68×10^{-1}	4.48×10^{-1}	2.02×10^{-3}	2.09×10^{-3}	2.16×10^{-3}	5.27×10^{-4}	1.57×10^{-3}	5.27×10^{-4}
1.0×10^{-5}	6.20×10^{-1}	7.51×10^{-1}	12.5×10^{-1}	2.45×10^{-3}	4.73×10^{-3}	1.79×10^{-3}	4.07×10^{-4}	3.26×10^{-4}	6.28×10^{-4}
5.0×10^{-6}	6.56×10^{-1}	14.9×10^{-1}	13.7×10^{-1}	8.53×10^{-4}	1.70×10^{-3}	4.24×10^{-3}	2.62×10^{-4}	1.59×10^{-4}	2.69×10^{-4}
1.0×10^{-6}	11.2×10^{-1}	4.78×10^{-1}	18.9×10^{-1}	1.93×10^{-4}	1.14×10^{-3}	3.16×10^{-4}	4.99×10^{-5}	5.47×10^{-5}	1.13×10^{-4}

Low values of selectivity coefficients were obtained which means no interfering of these cations on the electrode B response.

CONCLUSION

In this study, the constructions of new three electrodes of POP were based on poly (vinyl chloride) (PVC) membrane. It contains the ion-exchanger that formed between POP and BPB, using three different plasticizers: (DBPH), (TEHP) and (ONPOE). It was a sensitive, precise, rapid and inexpensive method which was used in the determination of POP in the pure form, pharmaceutical preparations and human fluids. The electrode B has shown a good performance with the time stability up to (42) days.

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