Preparation Pilocarpine Hydrochloride Selective Electrodes

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Abstract

New eight selective electrodes of pilocarpine hydrochloride deepened on complexes of (PCH) -molybdophosphoric acid and (PCH) – phosphotungstate were prepared with varied plasticizers. Electrode with complex (DBPH-MP) was used as an active material, gave linear range from 5.0×10^{-2} to 6.0×10^{-5} M, and slope was 62.01 mV/decade, with detection limit was 2.0×10^{-5}M, lifetime was near to 60 days. Electrode's membrane made with active material (DBP-MP), showed concentration range was 2.1×10^{-3}-6.3×10^{-5}M, the slope was near to 52.34 mV/decade. Detection limit was 1.0×10^{-5}M, 55 days was the life time of this electrode. The parameters of electrode deepened on (DBPH-PT), concentration range was from 5.0×10^{-2} to 6.5×10^{-5} M with slope 50.41 mV/decade, 2.2×10^{-5} M was the detection limit.Life time was determined around to 52 days.
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Keywords**:** Pilocarpine reactions, Sensors, membrane of PVC.

1. Introduction

Chemical name of Pilocarpine hydrochloride (PCH) is (3S,4R) Etheyl4-(1-methyl-1H-imidazol-5-ylmethyl4,5-dihydrofuran-2(3H)-one monohydrochloride, Pilocarpine hydrochloride exist as white crystal or powder, soluble in alcohol and water, practically insoluble in widely non-polar solvents, 244.72gm mol^{-1} has a molecular weight of it. It is used in treatment of glaucoma [1].

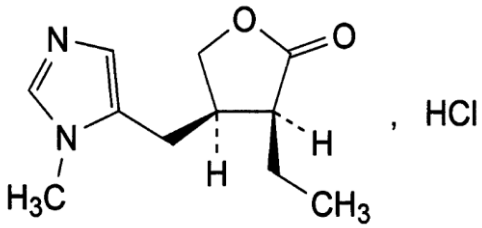

Fig.(1): Structure of pilocarpine hydrochloride.

Liquid chromatography Generality methods used to limitation of pilocarpine hydrochloride by using column: β- cyclodextrin [2], and in biological fluids [3]. First derivative were evaluated for pilocarpine hydrochloride by UV spectrophotometry at λ_1=222 nm and λ_2=307nm [4]. Measurements of mercuric content of pilocarpine complex by atomic absorption spectroscopic (AAS), the method was give recovery around (99.15±0.79)[5]. Spectrum of PCH, $C_{11}H_{17}N_2O_2Cl$ at 300K founded by (FT)-Raman spectrum and (FT-IR) spectrum [6]. For neutralization have need of a minimum quantity of alkali with PH=5 was used to constraction by used 93% of the unique pilocarpine [7]. Pilocarpine salt such as poly (methyl methacrylate) and nitrate, hydrochloride, onto) was studied as a sorption behavior [8]. Colorimetric method was optimized to determination of pilocarpine hydrochloride by control of time, concentration and PH, r =0.9800 with intercept 0.07 with slope=0.51[9]. Electrodes of pilocarpine deepened on PCH-tetrakis (4-chloro phenyl) borate and PCH-tetrakis [3,5 bis(triflouromethyl)-phenyl borate construction without internal reference solution, concentration rang was near to 3.0×10^{-5} and 6.0×10^{-5} to10^{-1}M, repectively [10]. Nernstian response for 4×10^{-5}- 10^{-1} M with PH about 4.0- 6.5 with good selectivity for PCH by using PVC matrix with (pilocarpine-reineckatc)ion pair complex, as an material electroactive [11].

2.1. Chemicals Details

High molecular weight poly(vinyl chloride)(PVC), Breon S110/10 B.P chemical U.K.Ltd, Tetrahydrofuran (THF) was from (BDH), Pilocarpine hydrochloride from State Company of Medical Appliances and Drug Industries (Samara IRAQ-SDI). Salagen, film coated (tablet, 5mg) product of

Chemical Industries Development Giza. phosphotungstate (PT), molybdophosphoric acid (MP), o-nitro phenyl octyl ether (o-NPOE), di-n-butyl phthalate (DBPH), tri-butylphosphate (TBP), di-n-butyl phosphate (DBP), were achieved from Fluka.PH effect was governed through using 0.1 M of sodium hydroxide and hydrochloric acid. Nearly analytical class chemicals and distilled water were used in experiments.

2.2. Standard Drug Solutions

Standard solutions 1×10^{-6} to1×10^{-1}M of Pilocarpine hydrochloride (PCH**)** were equipped by successive dilutions from standard solution (1×10^{-1} M) with spending distilled water.

2.3. Preparation Of ion-pair

Prepared Pilocarpine hydrochloride-Molybdophosphoric acid (PCH- MP) and Pilocarpine hydrochloride – phosphotungstate (PCH-PT) ion pairs via mixing 50 ml of 0.01M from drug(PCH) with 50 ml of 0.01M from Molybdophosphoric acid and50 ml of 0.01M from drug(PCH) with 50 ml of phosphotungstate, however stirring. Filtered the product precipitate and washed using water, at room temperature became dry.

2.4. Preparation of membrane

PVC membrane was equipped with mixed 0.04 g of (PCH-MP) with 0.36gm of plasticizers:(o-NPOE,DBP,TBP,DBPH). 0.17 g of PVC was mixed with 6-7 ml of THF, stirring until was be sticky solution. Then two solutions were mixed with stirring, and poured into a glass ring of (5 diameter) protected and left attitude over nighttime to let sublimation of the THF at room temperature [12]. From this membrane could prepare about 10 electrodes. Tube of glass was filled 3 /4 stock solution 0.1 M of drug M [13].

2.5. Equipment

1. Microprocessor, pH/mV/C Meter, pH211, HANA, Made in Romania.
2. Gallen Kamp (USA) as Calomel Reference Electrode.
3. Electrode of PH, H11131, HANA Instruments.
4. Conductance measurement founded by used conductivity meter type: Benchtop Conductivity Meter, TRANS Instruments, BC 302.

3. Results and Discussion

Results of electrode parameters acquired from the calibration graphs, are recorded in Table (1), and a typical calibration curve for the pilocarpine electrodes is shown in Chart.1, 2 for membrane E_1.The constancy of the eight electrodes was checked always by using pilocarpine hydrochloride at concentration 1.00×10^{-3}M of solution and assessed daily.

Table (1)
Pilocarpine hydrochloride electrodes responses.

Elec. No.	*Electrode membrane*	*Slope (mV/decade)*	*concentration range(M)*	*Detection limit(M)*	*Resp. time (sec)*	*Life time (day)*
E_1	PCH+MP+DBPH	62.01	5.0×10^{-2}-6.0×10^{-5}	2.0×10^{-5}	8	60
E_2	PCH+MP+DBP	52.34	2.1×10^{-3}-6.3×10^{-5}	1.0×10^{-5}	5	55
E_3	PCH+MP+TBP	47.44	6.2×10^{-3}-1.0×10^{-5}	5.0×10^{-2}	12	33
E_4	PCH+MP+NPOE	11.58	1.2×10^{-1}-5.5×10^{-3}	1.0×10^{-1}	7	19
E_5	PCH+PT+DBPH	50.41	5.0×10^{-2}-6.5×10^{-5}	2.2×10^{-5}	6	52
E_6	PCH+PT+DBP	37.30	6.5×10^{-1}-6.6×10^{-3}	3.3×10^{-1}	6	18
E_7	PCH+PT+TBP	11.49	1.0×10^{-4}-1.0×10^{-6}	1.0×10^{-4}	5	12
E_8	PCH+PT+NPOE	70.01	5.6×10^{-2}-9.7×10^{-4}	3.3×10^{-2}	3	7

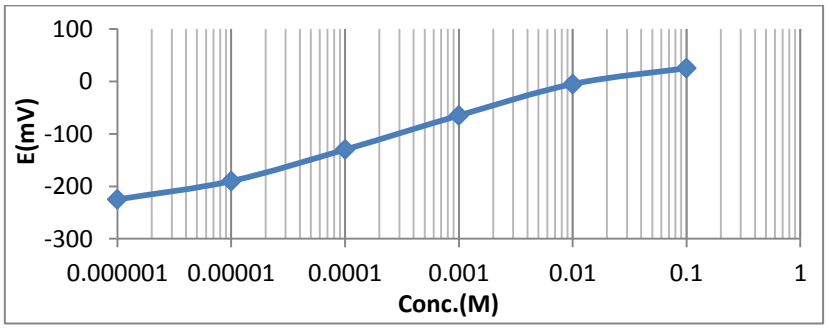

Chart (1): Response of electrode E_1.

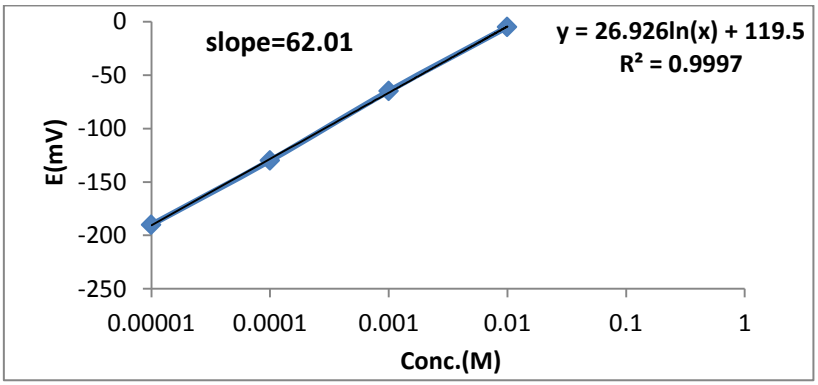

Chart (2): Calibration graph of electrode E_1.

Potential reply of the recommended electrode E_1 at changing concentrations of PCH donated a slope of 62.01 mV/decade, detection limit of 2.0×10^{-5} M, lifetime of close to 60 days. Conversely, membrane E_2, E_5 were gave away slopes 52.34, 50.41 mV/decade, respectively, and lifetime of around 55,52 day, respectively. Membrane E_8 donated a slope near to 70.01 mV/decade, 7 days was the lifetime this could be ascribed to the opposition of NPOE with the complex (PCH-MP) beginning outflow of the complex to the external solution from the membrane [14].

3.1. Effect of PH

PH effect of pilocarpine hydrochloride solutions for concentration 1×10^{-3} M on the response of the electrodes potential was investigated. The operational PH ranges are recorded in Table (2).

Table (2)
Range of PH for pilocarpine electrodes.

Electrode No.	Plasticizers	pH range
E_1	DBPH+MP	3.6-7.8
E_2	DBP+MP	2.3-7.8
E_5	DBPH+PT	3.0-7.8

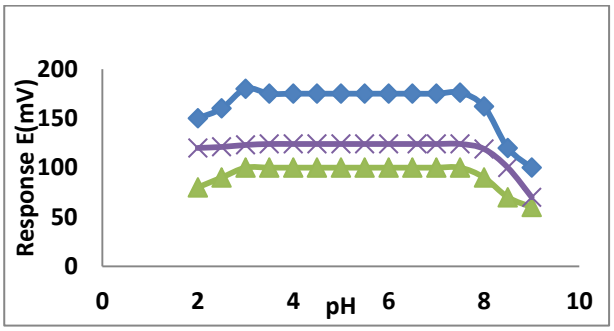

Chart (3): Response of pH effect for (PCH) electrodes at concentration 10^{-3} M of pilocarpine hydrochloride solution, ■ E_1,× E_2, ◢ E_5.

Characteristic plot for effect of pH on pilocarpine electrodes was presented in Chart.3. PH range of E_1 was about 3.6-7.8 and PH range for E_2 was 2.3 -7.8, PH for E_5 near to 3.0 -7.8; therefore, the suggested electrodes could be used to evaluating a wide series of pilocarpine concentrations. On the other hand, exterior this series the responses of electrodes change. Explicitly at pH values upper than 7.8 might be justified by removing the positive charge on the drug molecules [15]. At pH lesser than 2.0 (high acidity) response's electrode was amplified sporadically; because the electrodes reply became to activities of H^+ only.

3.2 Effect Of temperature

The temperature effect for electrodes with concentration from 10^{-6} to 10^{-2} M of pilocarpine solutions were studied in 25,30,35,40 ^{0}C. At dissimilar temperature were donated diverse of slope is stated in Table (3).

Table (3)
Different temperatures effect of pilocarpine electrodes.

No. of Electrode	Temperature ^{0}C	Slope (mV/decade)
E_1	25	62.01
	30	72.35
	35	81.23
	40	97.50
E_2	25	52.34
	30	65.10
	35	77.60
	40	100.43
E_5	25	50.41
	30	65.90
	35	75.12
	40	92.78

As of Table (3), it is apparent that a suitable Nernstian reply at temperatures 25-30^{0}C, electrodes, slope were leap to a very rising value at 40^{0}C (97.50, 100.43.92.78) m Vdecade^{-1}, respectively that might be quality to disintegration of ion pair.

3.3. Selectivity

Separate solution method were used to calculated the selectivity coefficient of the electrode from the reshuffled Nickolsky-Eisenman equation [16]:

$$\text{Log. } K^{pot}_{A,B} = [(EB - EA)\, z\, A\, F / 2.303\, RT] + (1 - z\, A / z\, B)\, \log a\, A.$$

The stimulus of some inorganic cations interfering for example Fe^{+3}, Al^{+3}, Mg^{+2}, Zn^{+2}, Na^{+1}, K^{+1} on the response of electrode as well considered Selectivity for electrodes E_1,E_2 and E_5, was estimated for concentration10^{-3}M with the separation method. The value of the selectivity coefficient for E_1, E_2 and E_5 electrodes are scheduled in Table (4) and selectivity of (PCH+MP+DBPH) electrode for interfering $K^{+1}$by separation method was shown in Chart.4.

Table (4)
Separate solution method (1×10^{-3} M of PCH and the interference) for determination Selectivity coefficient.

Interfering Ion	$K^{POT}_{A,B}$ for electrode E_1	$K^{POT}_{A,B}$ for electrode E_2	$K^{POT}_{A,B}$ for electrode E_5
Na^{+1}	8.076×10^{-3}	0.656	1.993
K^{+1}	6.347×10^{-3}	0.745	1.606
Mg^{+2}	1.852×10^{-2}	0.131	0.193
Zn^{+2}	5.405×10^{-5}	0.106	0.229
Fe^{+3}	1.175×10^{-5}	0.013	0.150
Al^{+3}	1.084×10^{-5}	9.588×10^{-3}	0.279

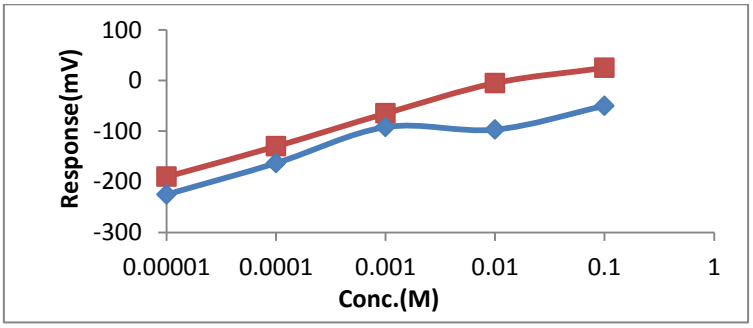

Chart (4): Interfering K^{+1} by separation method for (PCH+MP+DBPH) membrane, ■ –pilocarpine hydrochloride solution, ▪– solution of K^{+1}.

The selectivity coefficient were very small less than (0.1) for electrode E_1 and for ions Al^{3+}, $Fe^{+3}$of electrode E_2 with high selectivity coefficients for electrode E_5, the reason that selectivity of the ions-selective measuring device not only rely on the quality of ion exchanger, but as well meaningfully on the paste conformation, the nature of plasticizers and any spices expended, variances in mobility, ionic size, and porousness.

3.4. Analytical Applications

Conductometric and Titration methods to determination of PCH

A concentration of PCH prepared with transmitted to a beaker then dipped conductivity cell. Then added 10^{-3}M of MP and measured succeeding conductance. After each addition the evaluation was correct for thinning equation of conductivity method had a straight meaning of dilution [17].

$$\Omega corr = \Omega abs[V1 + V2/V1]$$

Ω is conductivity of electrolytic ,V1 = first volume, V2 = volume of the material corrected = corr. and observed = obs

A chart of revised conductivity opposed to volume of the supplemented titrant was formed. In quantitative conductometric this manner was used successfully showed in Chart (5), and titration method was used to determined pilocarpine hydrochloride by made titration between 1×10^{-3} M pilocarpine hydrochloride solution against 1×10^{-3} M of molybdophosphoric acid as a titrant shown in Chart.(6).

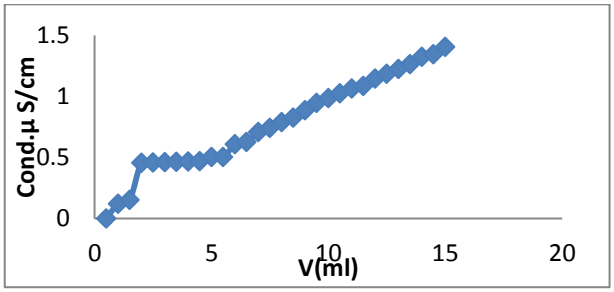

Chart (5): Conductivity measurements for (PCH+MP+DBPH) electrode.

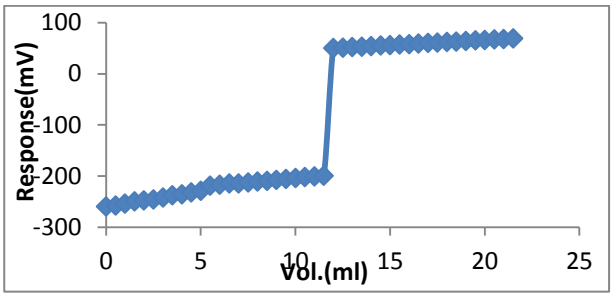

Chart (6): Titration curve for sample (1× 10^{-3}M) PCH with (1× 10^{-3}M) MP standard by electrode E1.

Upshots of the quantitative magnitudes for PCH solutions with relative error, relative standard deviations and recovery are recorded in Table (5) and Table (6).

Table (5)
Sample analysis using Conductometric and Titrtion methods for Pilocarpine hydrochloride solutions.

Type of Electrode	Type of Method	Concentration of Pilocarpine hydrochloride	RSD%	Er%	Re%
PCH+MP+DBPH (E_1)	Conductometric	1.00×10^{-3}	4.76	-1.23	98.77
	Titration	1.00×10^{-3}	0.96	2.06	102.06
PCH+PT+DBPH (E_5)	Conductometric	1.00×10^{-3}	7.57	-3.04	96.96
	Titration	1.00×10^{-3}	1.13	0.70	100.7

From statistical analysis of the piloarpine electrodes, was used for analysis of PCH in pharmaceutical formulations, RSD% were 4.76 and 7.57, respectively with Er% equal to -1.23 and -3.04, respectively ,and Re% were 98.77,96.96, respectively for conductometric method. Although for titration method RSD% were 0.96 and 1.13 with Er% equal to2.06, 0.70. Re% were 102.06 and 100.7.

Table (6)
Sample analysis using Conductometric and Titration methods for tablets Salagen solutions.

Type of Electrode	Type of Method	Concentration of Salagen	RSD%	Er%	Re%
PCH+MP+DBPH (E_1)	Conductometric	1.00×10^{-3}	0.06	1.00	101.00
	Titration	1.00×10^{-3}	1.00	-0.64	99.36
PCH+PT+DBPH (E_5)	Conductometric	1.00×10^{-3}	5.40	-5.41	94.59
	Titration	1.00×10^{-3}	1.29	-0.66	99.34

****n=3.***

Conductometric method for Salagen tablets, RSD% were 0.06 and 5.40, respectively, with Er% equal to 1.00, -5.41 respectively. Re% were about 101.00 and 94.59, respectively, and by titration method RSD% were 1.00, 1.29, respectively. Er% were -0.64 and -0.66, respectively, with Re% around 99.36 and 99.34, respectively. From these results could be analysis drugs by used potentiometric techniques.

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