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Synthesis Liquid Membrane Electrodes of Cephalexin Hydrochloride

Huda Ghalib Salman[1], Dalia M. Jamil[2], Amina M. Abass[3], Ahmed Ahmed[4]
[1,2,3,4]Department of Chemistry, College of Science, Al-Nahrain University, Al-Jaderia, Baghdad-Iraq.
Corresponding author: Amina M. Abass
E-mail: aminamohsen75@gmail.com

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ABSTRACT
A liquid cephalexin hydrochloride-sensors relied upon the ion pair of cephalexin hydrochloride(CEX) with phosphotungstic acid(PTA) are set up .The electrode shows a Nernstian slope 29.10 and 27.20 mV/decade for terminals relied upon NPOE and DOPH as a plasticizers in PVC lattice ,separately. Concentration extend were from 1.0×10^{-5} to 1.0×10^{-2} M for the two cathodes, the constraint of discovery were 6.5×10^{-6} and 4.0×10^{-6} M, separately. Relationship coefficient were 0.9994 and 0.9995 ,individually. Life time were 35 and 33 days ,separately ,additionally impact of PH were read for the two terminals. The new electrodes show great insight of cephalexin hydrochloride starting at various inorganic particles. The properties of the electrodes license it to exist utilized emphatically to assessment cephalexin hydrochloride stylish its medication plans.

Keywords: ion selective electrode, liquid membrane, PVC sensor, phosphotungstic acid, cephalexin hydrochloride.

Correspondence:
Amina M. Abass
Department of Chemistry, College of Science, Al – Nahrain University, Al – Jaderia, Baghdad, Iraq
E-mail: aminamohsen75@gmail.com

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INTRODUCTION

In pharmaceutical examination in most recent years, the potentiometric sensors have been far and wide go through, this is principally for the explanation that of little expense, basic plan, broad running of direct fixation run, little identification limit, adequate selectivity, high exactness ,and pertinence of the particular membrane electrode to turbid and shaded solutions[1]. Cephalexin is chemically(6R,7R)-7-[[(2R)- 2-amino-2-phenylacetyl]amino]-3-methyl-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic corrosive; hydrate; hydrochloride with atomic definition C16H17N3O4S1 with sub-atomic weight equivalent to 347.389 g/mole L. It is a white to grayish crystalline powder .Cephalexin is a semi manufactured original Cephalosporin antibacterial for the treatment of vulnerable contaminations just as those of respiratory tract, urinary tract and skin. It is powerful versus gram agreed and gram negative organism [2].

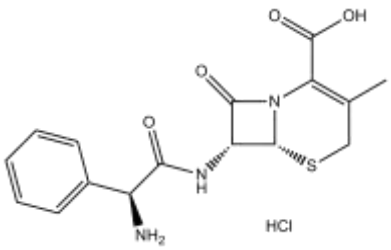


Figure 1: Structure of cephalexin hydrochloride.

To assurance cephalexin in drugs recipes, numerous concoction strategies were utilized, for example, spectrophotometer technique was set up for assurance of cephalexin in unadulterated equation and pharmaceutical details [3,4]. Elite meager layer chromatographic technique was created to investigation of cephalexin [5,6,7], also new method has been developed to validation of microbial bioassay for quantification of cephalexin in pharmaceutical formulations[8]. In aqueous two-phase system which counting cholinium chloride and potassium phosphate, the partitioning of cephalexin was evaluated[9].

Equipment

Potentiometric measurements were accomplished by using a digital millivoltmeter (Microprocessor, pH/mV/C Meter, pH211, HANA). PH works were complete with a digital PH meter (PH electrode, H11131, HANA, Made in Romania) underneath stirring conditions in temperature of room ($25.0\pm1.0C^0$). The performing of the membrane was explored by evaluating the EMFs of cephalexin solution through a range of concentration from 10^{-6} to 10^{-1} M by successive attenuation .Every one solution was stir up also the potential evaluation function of CEX of cation activities. The body of electrode were made-up and immobilized of cephalexin hydrochloride –Phosphotungustic acid (CEX-PTA) in PVC matrix membrane.

Reagents

At the first all the chemical used were reagent grade with in height purity and used as received without more cleansing, phosphotungestic acid (PTA) was acquired from (BDH), Tetrahydrofuran (THF) was provided from (BDH), cephalexin hydrochloride (CEX) was given from(IRAQ-SDI, Samara) Drug Industries and Medical Appliance and State Company .Cephalexin hydrochloride (containers BP 250 mg) provided from Ajanta pharma restricted APKEF. Plasticizers: Di-octylphenylphosphonate (DOPH), o-Nitro phenyl octyl ether (NPOE), were supplied from Fluka AG, Chemical PVC was provided from U.K .Ltd, type: Breon S110/10 B.P. From reserve arrangements which fixation 0.1M were set up of $AlCl_3$, $FeCl_3$, $CaCl_2$, $ZnCl_2$, NaCl, and LiCl, correlative diminished arrangements arranged by succeeding weakening of the arrangement. From Fluka, Aldrich and BDH, all synthetic concoctions mixes of expository were provided.

Synthesis of Ion-pair and Electrodes

Ion – pair was prepared by mixing solutions of phosphotungestic acid (PTA) with cephalexin hydrochloride (CEX) as following : 0.01M of ion – pair (PTA) with 0.01 M of drug (CEX) by weighting 0.3473 gm of cephalexin hydrochloride and 2.88005gm of phosphotungustic acid, then filtrate the finale solution with washing and let it to be dry in temperature of room[10].The system of arrest of the ion-pair composites hooked on the

PVC ground film as assigned by Graggs et al [11].A 0.04 gm of CEX-PT ionophore framework was admixed with 0.17 gm of PVC powder and 0.36gm of plasticizer. All were broken down in 6-7 ml of THF with blending while at the same time sitting tight for an unadulterated clingy arrangement was accomplished. The resultant arrangement into a glass throwing ring around 30 mm long and 35 mm in distance across .It consist of two pieces; one of them was glass plate and the other was the glass cylinder. The two pieces was gummed together by use THF- PVC sticky mixture to take care no loss in the membrane admixture. The high side of the tube was enclosed by using a filter paper. Then all of the contents were absent for two days to let deliberate vaporization of the solvent and establishment sensing membranes.

Adjustment of sensors

Standard arrangements of cephalexin which having scope of fixations around (10-1 - 10-6) mol/L were prepared. The estimations of mV for all of cephalexin arrangement was straightforwardly controlled by utilize the sensors. The estimations of focuses for cephalexin were arranged versus estimated possibilities and determined the inclines of the resultant normalization bends.

Selectivity

Selectivity of ion selective electrodes is quantitatively linked to equipoise at the interface stuck between the sample and electrode membrane [11].Furthermore, they are also necessary for the optimization of ion pair arrangements and membrane compositions. For example, errors increase when the reply to a feebly interfering ion is also influence by the main ion leak from the membrane. The selectivity coefficient in potentiometric methods is stated depended on the Nicolsky-Eisenman equation as: [12,13,14] to determine accurate potentiometric selectivity coefficients unaffected by such biases is:

$$E = E_0 + R\,T / Z_A F \ln [a_A + \mathbf{\Sigma K}_{A,B}(a_B)Za/Zb]$$

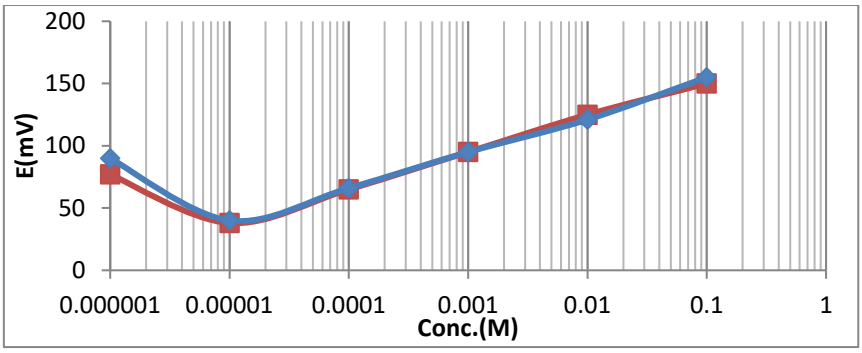
Which E is the deliberate potential; E0 is a consistent that contains the standard capability of the electrode, the reference terminal potential, (zA, zB, aA and aB are the charge numbers and exercises of the primary particle, An, and the meddling particle, B individually); and KA,B is the potentiometric selectivity coefficient for the meddling particle B versus the fundamental particle A. Selectivity coefficient can be likewise established by utilizing together match arrangements technique or separate arrangements, which contain together the meddling B particles also examiner A.

RESULTS AND DISCUSSION

Two membranes were set up as depicted in Table 1. The kind of membranes which plasticized with NPOE was gave a well reaction and also gave a lesser discovery limit than the other membrane, 6.5×10^{-6}, 4.0×10^{-6} M, separately. So it is famous, as far as possible for particle particular cathodes through disintegrated particle exchangers is estimated by the analyte particle focus part with in the arrangement as a finish of the circulation equalization of the particle pair stuck between the membrane and the arrangement [15]. The dissolvability of the particle pair in the natural dissolvable when all is said in done ascents as the dielectric steady ascents and polarization [16], which provide reason for the lesser discovery limit relied upon NPOE as plasticizer. The NPOE was painstakingly chosen for additional examinations. The alignment graphs, Schematic1, show the same reactions with together terminals, yet the recognition furthest reaches of electrode A (6.5×10^{-6} M) was littler than that of electrode B (4.0×10^{-6} M), on the grounds that the lesser grouping of cephalexin in the watery arrangement as a finale consequence of the appropriation balance of the particle exchanger.

Table1: Response of cephalexin hydrochloride electrodes (CEX-PTA)

Type of membrane	*CEX+ NPOE+PTA (A)*	*CEX+ DOPH+PTA (B)*
Range of Concentration (M)	1.0×10^{-5}- 1.0×10^{-2}	1.0×10^{-5}-$1.0\times10^{--2}$
Correlation coefficient (R)	0.9994	0.9995
Detection limit (M)	6.5×10^{-6}	4.0×10^{-6}
Slope (mV/decade)	29.10	27.20
Regre. Eq. Y = mX + b	Y=12.638ln(x)+18 2.6	Y=11.813ln(x)+175.7
Lifespan (day)	35	33



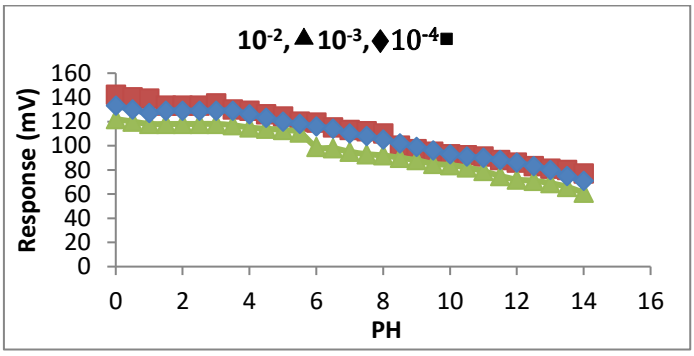
Schematic 1: Adjustment charts of Cephalexin obtained for the membranes A, B.

Influence of pH

Widespread application of an ion selective electrodes wants the data of the pH scope of the working of concurred terminal. The middle of the road corrosiveness might be influences the status of film segments and a particle partner [17]. The possibilities were recorded by three fixations (1.0 $\times 10^{-2}$, 1.0 $\times 10^{-3}$ and 1.0 $\times 10^{-4}$ M) of CEX+ particles as a component of pH for study the impact of pH on the procedure of the sensor. The pH of the arrangement was not at all like by the expansion of HCl and NaOH, the outcomes came to are appeared in Schematic 2.

Table 2: Impact of pH on the terminal potential for various cephalexin concentration

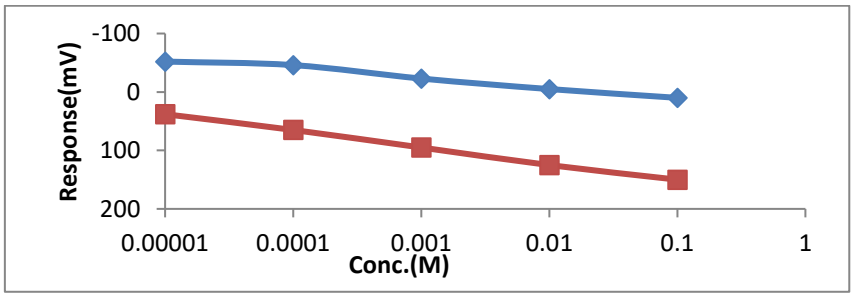
Type of membrane	Membrane composition	*pH range*		
		10^{-2}	10^{-3}	10^{-4}
A	*CEX+NPOE +PTA*	1.5-2.5	1.0-3.0	1.5-4.5
B	*CEX+DOPH+PT A*	1.5-3.0	2.0-3.5	2.5 -4.0



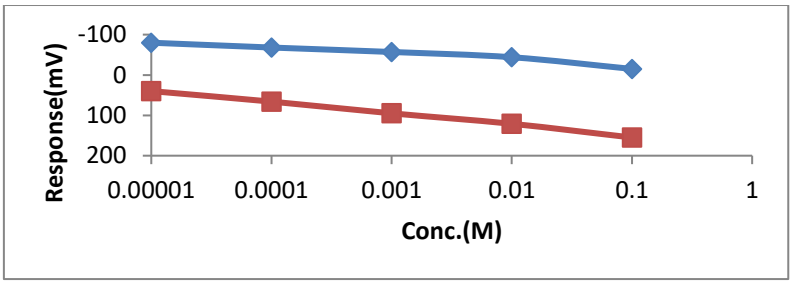
Schematic 2: Range of PH for cephalexin electrode A.

Selectivity

The selectivity of membrane electrode be dependent upon the physic-compound properties of particle trade strategy at the test arrangement – edge of membrane, on the development of the individual particles in the layer and on the hydrophobic communications stuck in the midst of the particles and the natural membrane [18].The selectivity of the cephalexin electrodes membrane is related to the free vitality of transmission of cephalexin cation among fluid and natural stages .The answer of the terminal was concentrated to a few changed inorganic particles more than once present in pharmaceuticals Li^{1+},Na^{1+},Ca^{2+},Zn^{2+},Fe^{3+} and Al^{3+},Schematic 3 shows the adjustment charts consenting to the assorted species dissected.



Schematic 3: Alignment diagram for cephalexin with interfere ion ($Li1^{+}$) for electrode A.



Schematic 4: Alignment diagram for cephalexin with interfere ion (Ca^{2+}) for electrode B.

Table 3: Selectivity coefficients determined for electrode A

Electrode A (CEX+NPOE+PTA)					
Concentration of Cephalexin hydrochloride					
Ion	10^{-5}	10^{-4}	10^{-3}	10^{-2}	10^{-1}
Li^{1+}	2.9267×10^{-5}	4.3362×10^{-4}	1.8333×10^{-4}	4.8212×10^{-5}	1.5452×10^{-5}
Na^{1+}	4.7051×10^{-3}	5.0797×10^{-4}	1.4459×10^{-4}	1.8657×10^{-5}	3.7191×10^{-6}
Ca^{2+}	6.5600×10^{-5}	1.5624×10^{-5}	3.5078×10^{-6}	4.1812×10^{-7}	9.0224×10^{-8}
Zn^{2+}	2.1496×10^{-4}	5.1200×10^{-5}	1.0098×10^{-5}	5.2597×10^{-6}	1.4390×10^{-6}
Fe^{3+}	8.2520×10^{-4}	9.6425×10^{-5}	3.4802×10^{-5}	4.4898×10^{-6}	1.1349×10^{-6}
Al^{3+}	9.6670×10^{-4}	2.3779×10^{-4}	8.3557×10^{-5}	1.2036×10^{-5}	3.1748×10^{-6}

Table 4: Selectivity coefficients determined for electrode B.

Electrode B(CEX+DOPH+PTA)					
Concentration of Cephalexin hydrochloride					
Ion	10^{-5}	10^{-4}	10^{-3}	10^{-2}	10^{-1}
Li^{1+}	2.5829×10^{-5}	6.1628×10^{-6}	3.4580×10^{-5}	3.0814×10^{-6}	7.1275×10^{-6}
Na^{1+}	2.2942×10^{-2}	4.6211×10^{-4}	6.8068×10^{-5}	1.0079×10^{-5}	1.1069×10^{-6}
Ca^{2+}	1.4041×10^{-4}	3.3502×10^{-5}	3.3428×10^{-8}	1.2143×10^{-6}	5.6234×10^{-7}
Zn^{2+}	7.1324×10^{-5}	8.5013×10^{-5}	4.0959×10^{-5}	6.0655×10^{-6}	1.5530×10^{-6}
Fe^{3+}	2.7175×10^{-3}	1.9488×10^{-3}	1.4582×10^{-4}	2.7837×10^{-5}	1.0902×10^{-6}
Al^{3+}	7.0135×10^{-4}	5.3027×10^{-4}	1.3612×10^{-5}	3.3536×10^{-6}	3.6827×10^{-7}

For pharmaceutical investigation, it is vivacious to check the selectivity to the excipients and the fillers added to the pharmaceutical details. A reasonable selectivity toward cephalexin within the sight of numerous inorganic cations was identified. The outcomes showed no basic obstruction by cephalexin pharmaceutical excipients. This is unadulterated as of the outcomes built up intended for the medication arrangements in Table 3,4 that these excipients don't meddle. Subsequently, the sensors have been seen as artificially idle to additional materials .The outcome is well than of those prior assigned for unmodified probes[19].

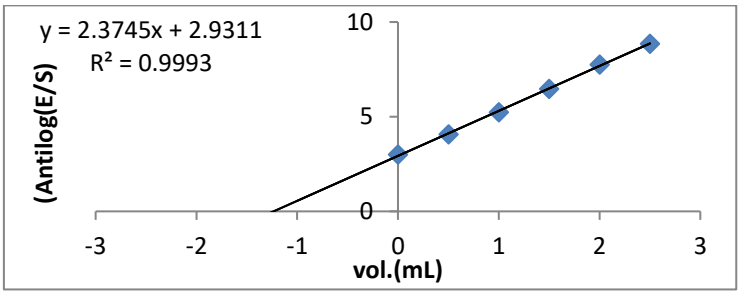
Analytical Appliances

The convergences of a fake arrangements of cephalexin were recorded utilizing a terminal relied upon NPOE and DOPH as plasticizers. For the assurance of cephalexin, four potentiometric strategies were utilized in particular, numerous standard expansion (MSA),standard expansion (SAM),direct, titration techniques [20,21]. The relative standard deviation RSD% and relative mistake RE% were compute for every single one of technique by utilize an anode relied upon NPOE and DOPH terminals. The % RSD, % Re, and % Er were planned and are enrolled in Table 5,6.

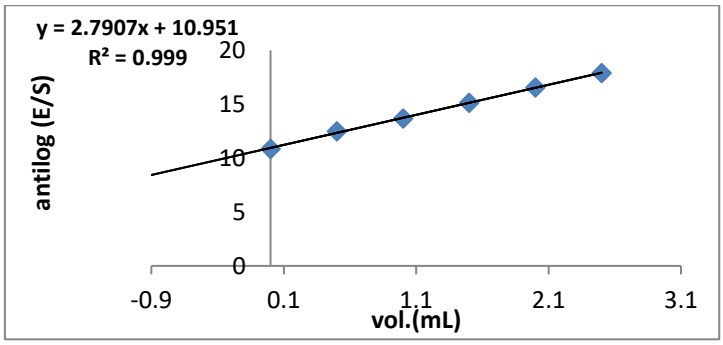
Table 5: Assurance of cephalexin in unadulterated cephalexin hydrochloride.

Electrode Type	Concentration(M)				
	Sample	Response by potentiometric method			
		Direct	SAM	MSA	Titration
CEX+NPOE+PTA	1×10^{-3}M	0.9645×10^{-3}	0.9655×10^{-3}	0.9778×10^{-3}	0.9564×10^{-3}
	RSD%	1.56-	3.62	-	
	Re%	96.45	96.55	97.78	95.64
	Er%	3.55-	-3.45	--2.22	4.36-
	1×10^{-4}M	0.9737×10^{-4}	0.9634×10^{-4}	0.9988×10^{-4}	0.9774×10^{-4}
	RSD%	-3.3	-2.37	-	
	Re%	97.37	96.34	99.88	97.74
	Er%	-2.63	-3.66	-0.12	-2.26

CEX+DOPH+PTA	1×10^{-3}M	0.9861×10^{-3}	0.9753×10^{-3}	0.9981×10^{-3}	0.9894×10^{-3}
	RSD%	0.38	0.16	-	-
	Re%	98.61	97.53	99.81	98.94
	Er%	-1.39	-2.47	- 0.19	-1.06
	1×10^{-4}M	0.9676×10^{-4}	0.96123×10^{-4}	0.9980×10^{-4}	0.9619×10^{-4}
	RSD%	1.58	-2.42	-	
	Re%	96.76	96.12	99.80	96.19
	Er%	3.24-	-3.88	-0.20	-3.81



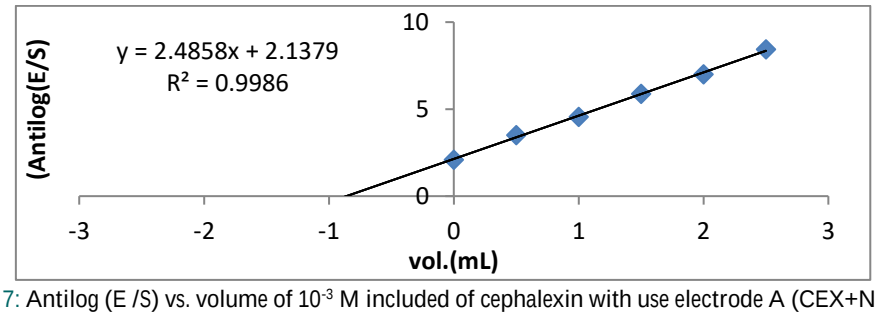
Schematic 5: Antilog (E /S) vs. volume of 10^{-3} M included of cephalexin with use electrode A (CEX+NPOE+PTA).



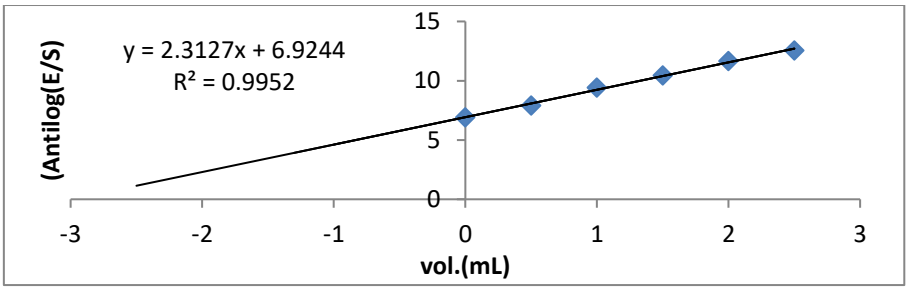
Schematic 6: Antilog (E /S) vs. volume of 10^{-3} M included of cephalexin with use electrode B (CEX+NPOE+PTA).

Table 6: Potentiometric procedures for investigation for cephalexin capsules.

Electrode Type	Concentration(M)				
	Sample	Response by potentiometric method			
		Direct	SAM	MSA	Titration
CEX+ NPOE+PTA	1×10^{-3}M	$\times10^{-3}$ 0.9647	0.9632×10^{-3}	0.9878×10^{-3}	0.9596×10^{-3}
	RSD%	0.64	0.38	-	-
	Re%	96.47	96.32	98.78	95.96
	Er%	-3.53	-3.68	-1.22	-4.04
CEX+DOPH +PTA	1×10^{-3}M	0.9743×10^{-3}	0.9876×10^{-3}	0.9914×10^{-3}	0.9744×10^{-3}
	RSD%	0.72	0.41	-	-
	Re%	97.43	98.76	99.14	97.44
	Er%	-2.57	-1.24	-0.86	-2.56



Schematic 7: Antilog (E /S) vs. volume of 10^{-3} M included of cephalexin with use electrode A (CEX+NPOE+PTA).



Schematic 8: Antilog (E /S) vs. volume of 10^{-3} M included of cephalexin with use electrode B (CEX+NPOE+PTA).

From table 5 cephalexin electrodes were have good recoveries for direct ,standard expansion ,multi standard addition, titration strategies equivalents to 96.45,96.55,97.78 and 95.64,respectively, with relative blunder close to-3.55,-3.45,- 2.22 and - 4.36,respectively,for cephalexin cathode relied upon NPOE as a plasticizer at fixation 10-3 M, and at focus 10-4 M for same terminal ,the recoveries were near to 97.37,96.34,99.88 and 97.74, respectively ,relative error were about to -2.63,-3.66,-0.12 and -2.26.For cephalexin electrodes based on DOPH as a plasticizer were gave recoveries for same methods above near to 98.61,97.53,99.81 and 98.94 ,respectively, at concentration 10^{-3} M of cephalexin solution with relative error equal to -1.39,-2.47,-0.19 and -1.06 respectively, while at concentration 10^{-4} M of cephalexin solution recoveries for same electrode were equal to 96.76,96.12,99.80 and 96.19 with relative error -3.24,-3.88,-0.20 and -3.81, respectively.

For Table 6 the values of recoveries were near to 96.47,96.32,98.78 and 95.96 ,respectively, with relative errors equal to -3.53,-3.68,-1.22 and -4.04 ,respectively, for cephalexin electrode based on NPOE at concentration of cephalexin solution 10^{-3} M .Electrode of cephalexin depended on DOPH as a plasticizer was gave good recoveries were about to 97.43,98.76,99.14 and 97.44,respectively and relative errors equal to -2.57,-1.24,-0.86 and -2.56,respectively.

CONCLUSIONS

Novel sensor was set up, relied upon a plasticized poly (vinyl chloride) (PVC) membrane containing the particle exchanger planned between phosphotungstic acid(PTA) and protonated cephalexin , gives a delicate, quick, exact and modest procedure for assessed cephalexin.

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REFERENCES

1. Bakhtiar Zadeh F.,Ab Gahani S.,(2008).Anion selective electrode for mercury(II) based on mercury (II) complex of poly (4-vinyl pyridine),J Electroanal.Chem., ,642:139-143.
2. Reddy G.R. et al.,(2017).Development and Validation of Microbial Bioassay for Quantification of Cephalexin in Pharmaceutical Preparations, Int. Res. J. Pharm.,8 (6).
3. Khan M.N. et al.,(2016).Development and Validation of a New Spectrophotometric Method for the Determination of Cephalexin Monohydrate in Pure Form and Pharmaceutical Formulations, J. Braz. Chem. Soc.,27(5) 912-918.
4. Ali Sh.M. . et al.,(2015). Spectroscopic Methods for Analysis of Cephalosporins in Pharmaceutical Formulations, World Journal of Analytical Chemistry,3(1A), 21-32.
5. Rahim N. et al.,(2015).Determination of Cefadroxil in Tablet/Capsule formulations by a validated Reverse Phase High Performance Liquid Chromatographic method, Pak. J. Pharm. Sci.,28 (4) :1345-1349.
6. Rijeb M.M.Al-Samarraee,(2015). High Performance Liquid Chromatographic Method for Determination of BromhexineHydrochloride in Pharmaceutical Syrups Sample, International Journal of Science and Research (IJSR), 6(5).
7. Bhinge S.D., Malipatil Sh.m.,(2016).Development and validation of a stability-indicating method for the simultaneous estimation of cefixime and dicloxacillin using the RP-HPLC method, Journal of Taibah University for Science 10 :734–744.
8. Reddy G.R. et al.,(2017) .Development and validation of microbial bioassay for quatification of cephalexin in pharmaceutical preparations ,Int.Res.J.Pharm,8(6).
9. Mokhtari A., Shahriari Sh.,(2017). Extraction of Cephalexin Using Aqueous Two-Phase Systems Composed of Cholinium Chloride and K3PO4, Journal of Applied Chemical Research, 11, 1, 21-33.
10. Abd El-Rhman M.K. et al.,(2017).Ion Selective Membrane Electrodes for the Determination of Mixture of Analgin and Camylofin Dihydrochloride in their Pure Form and Combined Dosage Form,Anal.Bioanal.Electrochem.,9(1):1-14.
11. Evans, A.,(1987).Potentiometry and Ion Selective Electrodes , John wiley & Sons.
12. Abass A.,M.,(2017).Synthesis New Liquid Selective Electrodes of Ciprofloxacin Hydrochloride for Determination Ciprofloxacin in Pure form and Pharmaceuticals Preparation", Baghdad Science Journal,14(4).
13. Abass A.,M.,(2017).Preparation Pilocarpine Hydrochloride Selective Electrodes, Journal of Al-Nahrain University ,20 (4):13-19.
14. Abass A.,M.,(2018).Preparation and Application of Tetracycline Hydrochloride Liquid membrane Electrodes, Journal of Al-Nahrain University,21 (2):73-80.
15. Koryta, J.; Stulik, K.(1983). Ion-Selective Electrodes, 2nd Ed.; Cambridge University Press: Cambridge, UK, 1983; p. 31.

16. Sekine, T.; Hasegawa, Y.(1977). Solvent Extraction Chemistry Fundamentals and Applications; Marcel Dekker: New York, NY, USA,p.149.
17. Kormosh Z, Hunka I, Bazel Y (2008) An electrode immobilized in a graphite matrix with ion pair complex for the determination of diclofenac in pharmaceuticals. J Iran Chem Res 1: 25-32.
18. Cosofret, V.V.; Buck, R.P.(1984). Phenothiazine drug poly(vinyl chloride) matrix membrane electrodes and their use in pharmaceutical analysis. Analyst ,109, 1321-1325.
19. Aki M.A., et al.,(2013). Construction of Modified Screen-Printed and Carbon Paste Electrodes for Electrochemical Determination of Antihistaminic Diphenhydramine Hydrochloride in Pure and Pharmaceutical Preparations, Int. J. Electrochem. Sci., 8:11546 – 11563.
20. Rundl Ch.(2004).A Beginners Guide to Ion Selective Electrodes Measurement , Nico Ltd. London, UK.
21. Mohammed H.A.,Abass A.A.," Poly (vinyl chloride) matrix membrane sensors for the quantification of cyclizine hydrochloride in pure and pharmaceutical preparations" AIP Conference Proceedings 2213, 020034 (2020); https://doi.org/10.1063/5.0000256