Construction of New Ion Selective Electrodes for Determination Chloramphenicol Sodium Succinate and Their Application in Pharmaceutical Samples

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Abstract

A liquid membrane electrodes for the determination chloramphenicol sodium succinate were constructed based on chloramphenicol palmitate and sodium tetraphenyl borate, and with four plasticizers, Di-butyl phthalate (DBPH); Di-butyl phosphate (DBP); Di-octyl phthalate (DOP); Tri-butyl phosphate (TBP); in PVC matrix. These electrodes give sub- Nernstian slopes (53.98, 51.45, 49.66 and 48.98 mV/decade) and linear ranges from ($1x10^{-4}$-$1x10^{-1}$, $5x10^{-4}$-$1x10^{-1}$, $1x10^{-4}$-$1x10^{-1}$, $5x10^{-4}$-$1x10^{-1}$ M) respectively. The best electrode was based on DBPH plasticizer which gave a slope 53.98 mV/decade, correlation coefficient 0.9999, detection limit of 5×10^{-5} M, lifetime 50 day displayed good stability and reproducibility and used to determine the Chloramphenicol sodium succinate in pharmaceutical samples. The measurement interferences in the presence of K^+, Na^+, Fe^{+3}, Al^{+3}, Cu^{+2}, Mn^{+2}, sucrose, Gelatine and Chloramphenicol palmitate were studied using the separated and mixed methods for selectivity coefficient determination. The pH and life time of the electrodes were also studied. The results were compared statistically with UV-spectrophotometeric technique by using F-test.

Keywords: Chloramphenicol sodium succinate selective electrodes, sodium tetraphenylborate, Chloramphenicol palmitate.

Introduction

Chloramphenicol palmitate (CPP), $C_{27}H_{42}Cl_2N_2O_6$, Fig.(1), a white or almost white , fine, unctuous powder with molecular weight 561.6 g/mole, practically insoluble in water, freely soluble in acetone , soluble in ether, sparingly soluble in alcohol, very slightly in hexane. It melts at 87°C to 95°C.[1] Chloramphenicol is a large spectrum antibiotic with antimicrobial activity. Its mechanism of action is based on the inhibition of protein synthesis. Chloramphenicol palmitate is quickly and almost completely hydrolyzed by intestinal esterase, being distributed widely throughout corporal liquids and quickly achieving therapeutic levels.[2]

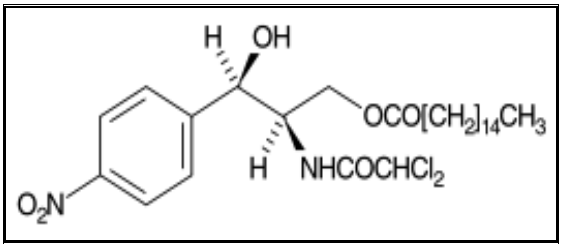


Fig.(1) Structure formula of chloramphenicol palmitate.

Chloramphenicol sodium succinate (CPSS) is a white or yellowish-white powder, hygroscopic, very soluble in water, freely soluble in alcohol, practically insoluble in ether. chloramphenicol sodium succinate has a molecular weight of 445.2, its molecular formula is $C_{15}H_{15}Cl_2N_2$ NaO_8 and it's structural formula as shown in Fig.(2).[3]

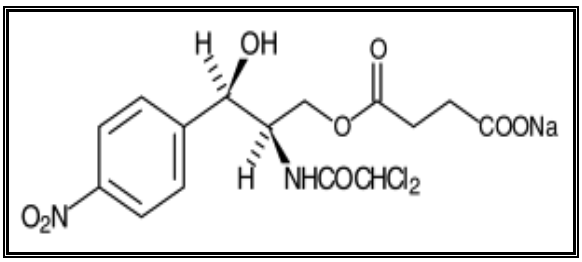


Fig.(2) Structure formula of Chloramphenicol sodium succinate.

Several methods have been reported for the determination of chloramphenicol sodium succinate has been reported in the literature, including spectrophotometric[4] and liquid chromatographic methods[5,6]. The applications of ion selective electrodes continue to be of interest in pharmaceutical analysis because

these sensors offer the advantages of simple design and operation, reasonable selectivity, fast response, low cost and applicability to turbid and colored solutions. In this work the sensor is based on chloramphenicol palmitate and sodium tetraphenylborate as additive in polyvinyl chloride plasticized with DPPH plasticizer was used for the determination Chloramphenicol sodium succinate and compare with UV derivative spectrophotometry

Experimental

Equipment

An expandable ion analyzer (Orion model EA-940, USA), a pH meter (WTW model pH 522, Germany), Double beam UV-Vis spectrophotometer model (UV-1650 PC) SHIMADZ (Japan) and a Silver-silver chloride electrode were used in this work.

Chemicals and Reagents

Polyvinyl chloride (PVC) of relatively high molecular weight (Breon S 110/10 B.P Chemical U. K. Ltd).

Chloramphenicol palmitate (CPP) and Chloramphenicol sodium succinate (CPSS) standard from (Samara IRAQ-SDI). Chloramphenicol sodium succinate injection (1.00g) made in (Humberg-Germany). (DBP), (DBPH), (DOP) and (TBP) were purchased from Fluka AG, Switzerland, Tetrahydrofuran (E.Merck). Other chemicals and solvents were of an analytical reagent grade obtained from BDH, Stock solutions of 0.1 M for each of NaCl, KCl, $CuSO_4$, $MnSO_4$, $Fe_2(SO_4)_3.9H_2O$, $AlCl_3.6H_2O$, sucrose, gelatin and CPP were prepared by dissolving 0.2922, 0.3729, 0.7980, 0.7550, 0.1265, 1.2075, 1.7115, 1.50 and 2.8077 in 50 mL of distilled water respectively.

A stock standard solution of 0.1 M chloramphenicol sodium succinate was prepared by dissolving 2.226 g of standard solution and making the solution up to 50 mL with distilled water. The working solutions 10^{-7}-10^{-1} M CPSS were prepared by serial appropriate dilution of the stock solution.

A standard solution of 0.01 M Sodium tetraphenylborate (TPB) was prepared by dissolving 0.1746 g of pure (TPB) in distilled water and completing the solution up to 50 mL. Stock solution of 0.1 M of HCl and 0.1 M of NaOH which are used for adjusting pH of solutions.

Procedure

Construction of ion-selective electrodes

The construction of the electrode body and the immobilization were done as described by Mahajan et al [7]. The glass tube was 3/4 filled with 0.01 M chloramphenicol sodium succinate solution as an internal filling solution. The membrane was conditioned by immersing in a standard solution of 0.1M chloramphenicol sodium succinate for at least 2 hour before measurements.

Preparation of Pharmaceutical Samples

All contents of 10 vial chloramphenicol sodium succinate 1.00g dissolved in 1L distilled water, the resultant solution is $2.2x10^{-2}$ M. Other samples prepared by serial dilution.

Calculation of Selectivity coefficient

A separate solution method [8] was used for the selectivity coefficient measurement, which calculated according to the equation:

$$\log K^{pot}_{A,B}=(E_B-E_A)/S+(1-z_A/z_B)\log a_A \quad \ldots\ldots\ldots(1)$$

E_A, E_B; z_A, z_B; and a_A, are the potentials, charge numbers, and activities for the primary A ion, respectively, at $a_A = a_B$.

The selectivity coefficients were also measured by the mixed method (Fixed interference method) [9,10] according to the equation:

$$K^{pot}_{A,B}=a_A/(a_B)^{zA/zB} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots(2)$$

Results and Discussion

Four electrodes of chloramphenicol sodium succinate (CPSS) (A1, A2, A3, A4) based on using chloramphenicol palmitate (CPP) and tetraphenylborate (TPB) as additive, used four plasticizers such as: Di-butyl phthalate (DBPH); Di-butyl phosphate (DBP); Di-octyl phthalate (DOP); Tri-butyl phosphate (TBP); with PVC matrix were examined respectively. Non-Nernstian slopes were obtained for electrodes based on DBP, DOP and TBP (membranes A2, A3 and A4).The slopes are 51.45, 49.66 and 48.98 mV/decade with correlation coefficients of 0.9993, 0.9990 and 0.9998 respectively. The linear range for these electrodes $5x10^{-4}$-$1x10^{-1}$, $1x10^{-4}$-$1x10^{-1}$ and $5x10^{-4}$-$1x10^{-1}$ M

with detection limits of $2x10^{-5}$ M, $3x10^{-5}$ M and $1x10^{-5}$ M, respectively. The results and other parameters are given in Table (1). The electrode (A4) gave non-Nernst slope, this could be due to the low viscosity of TPB (3.114 cst) which causes rapid leaching of the membrane components to the external solution. The electrode (A2), gave slope of 51.45 mV/decade due to the viscosity of the plasticizers; for example, the high viscosity of the DBP (112.88 cst) plasticizer which decrease the ion-exchange process between (CPP) in membrane and the external solution of (CPSS). Then the A3 electrode gave slope 49.66 mV/decade, due to inhomogeneous gradients between (DOP), (PVC) and other components in the membrane[11]. The sensor (A1) displays a linear response from 10^{-4} to 10^{-1}M (CPSS) with sub-Nernstian cationic slope of 53.98 mV/decade with lower limit of detection of $5x10^{-5}$ M, which was calculated at the point of intersection of the extrapolated segments of the two linear parts of the calibration curve of (CPSS). Electrode (A1) gave high slope value because the high mixing between the (DBPH) and the poly phenyl chloride (PVC) due to the compatibility of the plasticizer used to the electro-active compound in both structure and composition. A typical plot for calibration curves of electrodes based on four plasticizers DBPH, DBP, DOP and TBP are shown in Fig.(3).

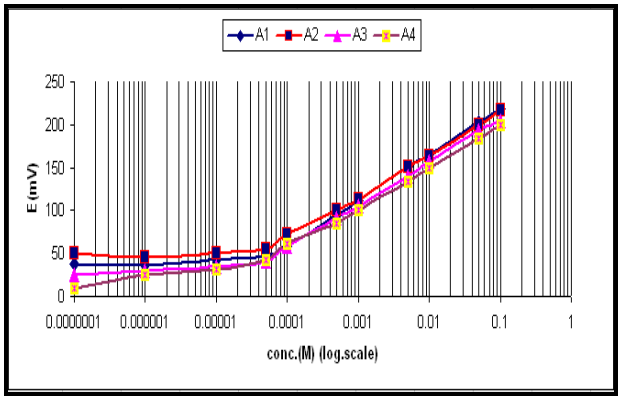


Fig.(3) Calibration curves of Chloramphenicol sodium succinate selective electrodes using DBPH, DPB, DOP and TBP plasticizer.

Table (1)
The parameters for four (CPSS) electrodes.

Electrode	*Slope (mV/Decade)*	*Linear equation*	*Correlation coefficient (r)*	*Linear concentration range (M)*	*Detection limit (M)*	*Response time (sec)*			*Lifetime (day)*
						10^{-2} (M)	*10^{-3} (M)*	*10^{-4} (M)*	
A1 CPP+TPB+DBPH	**53.98**	**y = 23.442 Ln(x) + 273.50**	**0.9999**	1×10^{-4}– 1×10^{-1}	5×10-5	25	15	10	50
A2 CPP+TPB+DBP	**51.45**	**y = 22.341 Ln(x) + 267.81**	**0.9993**	5×10^{-4}–1 $\times10^{-1}$	2×10-5	30	18	12	15
A3 CPP+TPB+DOP	**49.66**	**y = 21.564 Ln(x) + 255.47**	**0.9990**	1×10^{-4} –1×10^{-1}	3×10-5	35	20	14	23
A4 CPP+TPB+TBP	**48.98**	**y = 21.272 Ln(x) +247.54**	**0.9998**	5×10^{-4}– 1×10^{-1}	1×10-5	45	35	15	21

Effect of pH:-

The effect of pH on the electrode potentials for (CPSS) selective membrane electrode (A1) was examined by measuring the e.m.f. of the cell in (CPSS) solutions at three different concentrations (10^{-4}, 10^{-3}, 10^{-2}) M in which the pH ranged from (0.5-11.0). The pH adjusted by adding appropriate amounts of hydrochloric acid and/or sodium hydroxide solution. The results shown in Fig.(4)

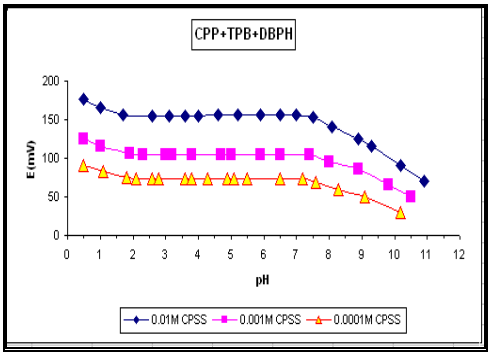


Fig.(4) Effect of pH on the potential of the electrode A1 at concentrations 10^{-2}, 10^{-3} and 10^{-4} M.

At pH values less than 1.5 or in very high acidity, the electrode response has been increased rather irregularly. This may be due to that the electrode response to H^+ activities as well as CPSS ions and in an alkaline solution (pH greater than 8) the electrode response has been decreased, may attribute to the decreasing in the solubility of CPSS.[12] The working pH were tabulated in Table (2).

Table (2)
Working pH ranges for CPSS electrode (A1).

Electro de no.	*Composition of electrode A1*	*PH range*		
		10^{-2}	10^{-3}	10^{-4}
A1	CPP+TPB+DBPH	1.5-7.5	2.0-7.5	2.0-7.2

Interference studies

In order to investigate the selectivity of the proposed membrane (A1) ion selective electrode toward chloramphenicol sodium succinate with respect to various interfering ionsby using separate solution method. The values of the selectivity coefficients for separate method are listed in Table (3).

In Fixed interference method, the potential values obtained are plotted vs. the logarithm of the concentration of the chloramphenicol sodium succinate. The intersection of the extrapolated linear portions of this plot indicates the chloramphenicol sodium succinate. The intersection of the extrapolated linear portions of this plot indicates the value of (a_A) as shown in Fig.(5). The results of selectivity coefficients listed in Table (3), the data refer is the interfering species tested don't significantly influence the potentiometric response of the proposed PVC-membrane electrode toward chloramphenicol sodium succinate.

Table (3)
Values of $K^{pot}_{A,B}$ according to separate method and FIM by using electrode A1.

Interfering ions	*Separate method*	*FIM*	
		$a_B=5\times10^{-2}$	
		a_{CPSS}	$K^{pot}_{A,B}$
k^+	2.49×10^{-2}	1.4×10^{-4}	2.80×10^{-3}
Na^+	3.36×10^{-2}	5.0×10^{-4}	1.00×10^{-2}
Fe^{+3}	7.09×10^{-4}	5.0×10^{-5}	1.34×10^{-4}
Al^{+3}	5.73×10^{-4}	9.5×10^{-6}	2.55×10^{-5}
Cu^{+2}	1.49×10^{-3}	4.4×10^{-5}	1.96×10^{-4}
Mn^{+2}	9.37×10^{-3}	1.5×10^{-5}	6.70×10^{-5}
Sugrose	8.24×10^{-2}	3.0×10^{-5}	6.00×10^{-4}
Gelatine	5.86×10^{-2}	2.0×10^{-5}	4.00×10^{-4}
CPP	8.91×10^{-2}	2.0×10^{-5}	4.00×10^{-4}

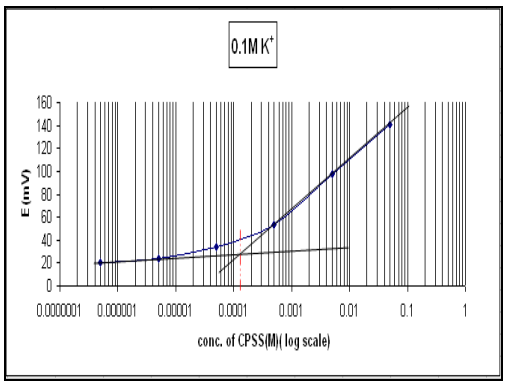


Fig.(5) Calibration curve of fixed interfering method chloramphenicol sodium succinate selective electrode (A1).

Sample analyses:-

Four potentiometric techniques were used for the determination of (CPSS) including. Direct method, Standard addition method (SAM) follows the equation:

$C_U = C_S / 10^{\Delta E/S} [1+ (V_U / V_S)] - (V_U / V_S)$

Where C_U, C_S, V_U and V_S are the concentration and volume of unknown and standard solution respectively Multiple standard additions (MSA) carried as in Fig.(6). by plotting antilog (E/S) versus the volume of the five addition of standard (CPSS), used to of concentration can be covered as compared with working range calibration curve for MSA

used to determine the concentration of chloramphenicol sodium succinate solutions. For potentiometric titration a 10^{-2} M of tetraphenyl borate were used as a titrant. A typical titration plot was shown in Fig.(7).

The recovery (Re %), relative error (E_r %) and relative standard deviation (RSD %) for each method are calculated and the results are listed in Table (4).

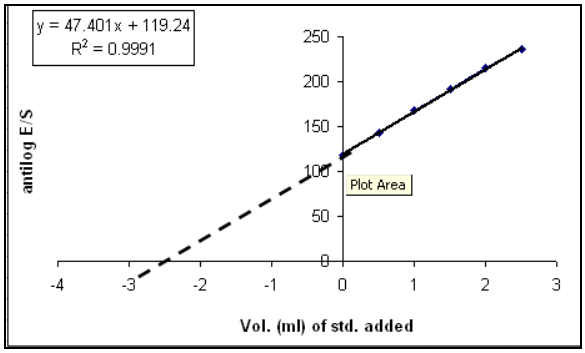
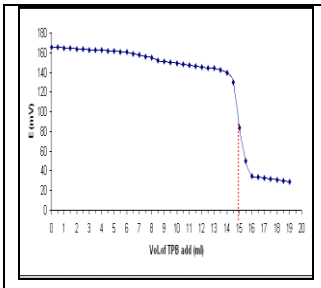
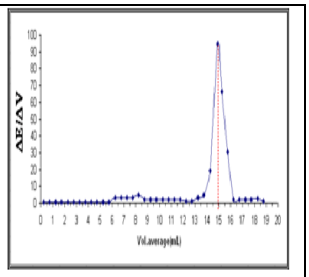


Fig.(6) Plot of antilog (E/S) versus the volume of chloramphenicol sodium succinate using A1 electrode.



Titration curve using electrode (A1).



First derivative Titration curve using electrode (A1).

Fig.(7) Titration curves of chloramphenicol sodium succinate selective electrode using DBPH plasticizer.

The electrode (A1) was proved to be useful in the potentiometric determination of chloramphenicol sodium succinate in pharmaceutical preparations and the data obtained for pharmaceutical samples were listed in Table (5).

Table (4)
Analysis of CPSS by potentiometric techniques by using ISE A1.

Parameter	*Direct method*	*SAM*	*MSA*	*Titration Method*
Conc.(M)	**1.000×10^{-4}**	**1.000×10^{-3}**	**1.000×10^{-3}**	**1.000×10^{-2}**
Found(M)	**0.996×10^{-4}**	**1.001×10^{-3}**	**1.006×10^{-3}**	**0.9895×10^{-2}**
RSD%*	**0.477%**	**0.754%**	----------	**0.500%**
Re%	**99.6%**	**100.1%**	**100.6%**	**98.9 %**
relative error%	**-0.4%**	**0.1%**	**0.6%**	**-1.1 %**

Table (5)
Sample analyses of chloramphenicol sodium succinate injection pharmaceutical.

Parameter	*Direct method*	*SAM*	*MSA*	*Titration Method*
Conc.(M)	1.000×10^{-3}	1.000×10^{-3}	1.000×10^{-3}	1.000×10^{-3}
Found(M)	0.998×10^{-3}	1.001×10^{-3}	1.004×10^{-3}	0.999×10^{-3}
RSD%*	0.668%	0.906%	----------	0.919 %
Re%	99.8%	100.1%	100.4%	99.9 %
E_r%	-0.2%	0.1%	0.4%	-0.1 %
S	6.671×10^{-6}	9.071×10^{-6}	----------	----------
$\overline{x} \pm (ts/\sqrt{N})$	$0.998\times10^{-3}\pm0.829\times10^{-5}$	$1.001\times10^{-3}\pm0.112\times10^{-4}$	----------	----------

RSD*% for n=5, t=2.7

Sample analyses by using UV spectrophotometry:-

Normal UV spectrum of chloramphenicol sodium succinate (CPSS) show the absorption wavelength 276 nm. Fig.(8) shows the spectra for solutions ranged from 2-64 mg/L of CPSS. The calibration curve for CPSS at 276 nm has linear equation of the (Y=0.01002X+0.48860), which show high back ground but can be determine the concentration of the unknown samples with the above linear range, and confidence limit (t 95%). The results of 10^{-4}M CPSS are listed in Table (6).

First Derivative (^{1}D):-

Fig.(9), shows First-derivative (^{1}D) spectra for CPSS solutions 2-64 mg/L have been taken from normal using scale factor=10, CPSS. First-derivative spectrum shows a fixed peak (P) at 258 nm and fixed valley (V) at 300 nm. But all peaks and valleys below 220 nm gave a noisy signal.

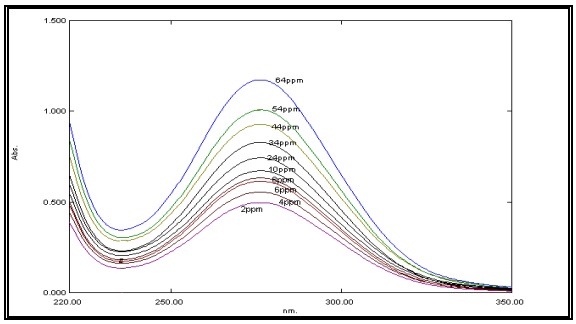


Fig.(8) Spectra for CPSS solutions at different concentration ranged from 2-64 mg/L.

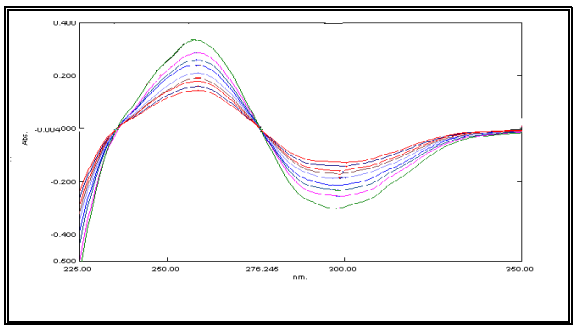


Fig.(9) The first derivative spectra for CPSS solutions 2-64 mg/L.

Comparison between ISE and normal spectroscopy and first derivative (^{1}D) methods:-

The results of comparison between normal spectroscopy and first derivative (^{1}D) with direct method of ion selective electrode by using F-test are shown in the Table (6 and 7) respectively. The analytical methods results were showed to be simple, rapid and with a good precision by comparing between normal spectroscopy and first derivative (^{1}D) with direct method of ion selective electrode by using F-test at 95% confidence limit. Since $F_{calculated} < F_{Tabulated}$ .therefore there is no significant difference in precision between the proposed method and spectrophotometric methods.

Table (6)
Calculation of F-test between the two methods ISE and UV-spectrophotometry.

C_U(M) from direct method of ISE	S*	C_U(M) from direct method of UV-spectrophotometry	S*	The (F) magnitude	
				calculated	Tabulated
0.996×10^{-4}	4.764×10^{-7}	0.989×10^{-4}	6.221×10^{-7}	1.7052	6.39
0.998×10^{-4}		0.995×10^{-4}			
0.995×10^{-4}		0.998×10^{-4}			
0.991×10^{-4}		1.002×10^{-4}			
1.004×10^{-4}		1.005×10^{-4}			

S*: standard deviation; n= 5, F= S_1^2 / S_2^2, where $S_1 > S_2$.

Table (7)
Calculation of F-test between the two methods ISE and first derivative.

C_U(M) from direct method of ISE	S*	C_U(M) from direct method of First Derivative	S*	The (F) magnitude	
				Calculated	Tabulated
0.996×10^{-4}	4.764×10^{-7}	0.991×10^{-4}	6.942×10^{-7}	2.1233	6.39
0.998×10^{-4}		1.005×10^{-4}			
0.995×10^{-4}		0.997×10^{-4}			
0.991×10^{-4}		1.007×10^{-4}			
1.004×10^{-4}		1.006×10^{-4}			

S*: standard deviation; n= 5, $F = S_1^2 / S_2^2$, where $S_1 > S_2$, $F_{table}=6.39$.

Conclusions

ISE method included fabrication of membranes for chloramphenicol sodium (CPSS) succinate was constructed based on using chloramphenicol palmitate (CPP) and sodium tetraphenylborate (TPB) as additive and many plasticizers. The best electrode for CPSS was (A1) electrode which used to determine CPSS in the pharmaceutical samples (chloramphenicol sodium succinate injection). Also there is no interference for some interfering ions. The proposed analytical method is proved to be simple and rapid, with good accuracy. Chloramphenicol sodium succinate can be determined by using Ion selective electrode method by using F-test, By comparison between ion selective electrode with normal and derivative spectroscopy methds.

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الخلاصة

حضرت أقطاب انتقائية سائلة لتقدير الكلورامفينيكول صوديوم ساكسينيت والتي تعتمد على للكلورامفينيكول صوديوم بالميتيت والصوديوم تيترافنيل بوريت مع أربعة من الملدنات, داي بيوتيل فثاليت، داي بيوتيل فوسفيت, داي اوكتيل فثاليت وتراي بيوتيل فوسفيت بوليمر الفاينيل كلورايد على التوالي. اعطت هذة الأقطاب انحدارا شبه نيرنيستي 53.98, 51.45 , 49.66 و 48.98 ملي فولت/ حقبة ومدى التركيز الخطى حوالي من 10^{-4} الى 10^{-1} . وكان أفضل قطب الذي يعتمد على داي بيوتيل فثاليت كملدن حيث اعطى انحدارا 53.98، معامل ارتباط 9999، حد كشف $5X10^{-5}$ وعمره 50 يوم مع استفرارية وتكرارية جيدة، لتقدير الكلورامفينيكول صوديوم ساكسينيت في المستحضرات الصيدلاتية. كذلك درست التدخلات لحساب معامل الانتقائية بطريقة المحاليل المنقصلة وطريقة المحاليل الممزوجة بوجود الايونات المواد التالية (K^+, Na^+, Fe^{+3}, Al^{+3}, Cu^{+2}, Mn^{+2}, sucrose, Gelatine and Chloramphenicol palmitate) ودراست حدود الدالة الحامضية وعمر القطب. حيث تمت مقارنة النتائج مع الطريقة ا لطيفية من خلال اجراء الـــ F-test.