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Ministry of Higher Education and Scientific Research
Al-Nahrain University
College of Science
Department of Chemistry

Construction of new Ion Selective electrodes for Determination Chloramphenicol sodium succinate and Iron(III) and their applications in pharmaceutical samples

A Thesis submitted to the College of Science Al-Nahrain University in partial fulfillment of the requirements for the Degree of Master of Science in Chemistry

By
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بِسمِ اللهِ الرحمنِ الرحِيمِ

ربناءاتِنا مِن لدنك رحمةً وهيئ

لنا مِن امرِنا رشدا

صَدقَ اللهُ العَظيم

سورة الكهف / جزء من اية 10

الإهداء

إلى الدي لم يال جهدا في تربيتي مند الصغر ..... ابي الغالي

إلى التي ندرت شبابها من اجلي ..... امي الغالية

الى من غرس في نفسي الامل الى القلب الكبير .....زوجي الغالي

إلى سمسي وضياء نهاري .....بنايتي (سمس..همس)

إلى من هم بلسم جراحي ..... اخوتي واخواتي

إلى كل من فرح بي وشجعني على هده الدراسة ..... الاصدقاء والاقارب

إليهم جميعا اهدي ثمرة جهدي عرفانا بفضلهم .....

وئام

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I certify that this thesis was prepared under my supervision at the Department of Chemistry, College of Science, AL- Nahrain University as partial requirements for the Degree of Master of Science in Chemistry.

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We, the Examining Committee, certify that we have read this thesis and examined the student (Weam Raad Azeez) in its contents, and that in our opinion it is adequate with ( ) standing as a thesis for the Degree of Master of Science, in Chemistry.

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Weam Raad Azeez

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Contents

Summary:-

Two kinds of electrodes were prepared in this study based on PVC matrix. Four ion selective electrodes for Chloramphenicol sodium succinate which based on chloramphenicol palmitate (CPP) and sodium tetraphenylborate (TPB) as additive, Another Four ion selective electrodes for Iron(III) based on Chloramphenicol sodium succinate-Iron(III) [CPSS-Fe(III)] ion-pair complex as the electro-active material,. Many plasticizers used:

- Di-butyl phthalate (DBPH)
- Di-butyl phosphate (DBP)
- Di-octyl phthalate (DOP)
- Tri-butyl phosphate (TBP)

The electrodes parameters were include, linear concentration range, Nernestian slope, limit of detection, response time, life time, working pH rang and selectivity were evaluated. Also the statistical treatments were applied for the results that include: relative standard deviation (RSD), relative error (RE), error and confidence limit for concentration. The results showed:

1- ISE_S for Chloramphenicol sodium succinate:

CPP+TPB+DBPH (membrane A1), CPP+TPB+DBP(membrane A2), CPP+TPB+DOP (membrane A3), CPP+TPB+TBP (membrane A4), gives the slopes (53.98, 51.45, 49.66 and 48.98 mV/decade), linear range from ($1x10^{-4}$-$1x10^{-1}$, $5x10^{-4}$-$1x10^{-1}$, $1x10^{-4}$-$1x10^{-1}$, $5x10^{-4}$-$1x10^{-1}$), with detection limit ($5x10^{-5}$M, $2x10^{-5}$ M, $3x10^{-5}$ M and $1x10^{-5}$ M), response time of 10^{-3} M (15, 18, 20 and 35 second) and the lifetime were about (50, 15, 23 and 21 day). The working pH ranges were ranged from (2–7.5). The electrode A1 (CPP+TPB+DBPH) has been used to determine

Chloramphenicol sodium succinate in the pharmaceutical samples of (Chloramphenicol sodium succinate injection).

2- ISE_S for Iron(III):

CPSS-Fe(III)+DBP (membrane B1), CPSS-Fe(III)+DBPH (membrane B2), CPSS-Fe(III)+DOP (membrane B3) and CPSS-Fe(III)+TBP (membrane B4), gives the slopes (19.79, 26.60, 16.01 and 13.82), linear range from ($1x10^{-5}$- $1x10^{-2}$ M, $1x10^{-5}$-$1x10^{-2}$ M, $1x10^{-6}$-$1x10^{-2}$ M and $1x10^{-5}$-$1x10^{-2}$ M), with detection limit (9×10^{-6} M, 7×10^{-5} M, 2×10^{-6} M and 9×10^{-5} M), response time of 10^{-3} M (10, 35, 15, 35 and 30 second), lifetime were about (37, 41, 23 and 16 days). The working pH ranges were ranged from (2 - 6) by using electrode (CPSS-Fe(III)+DBP), and this electrode has been used to determine Iron(III) in the pharmaceutical samples of (Feroglobin Capsules).

The selectivity coefficients ($K^{pot}_{A,B}$) of ISE_S have been studied for the following interference ions (Na^+, K^+, Mn^{+2}, Cu^{+2}, Zn^{+2}, Fe^{+3}, Al^{+3}, Chloramphenicol palmitate, folic acid , Sucrose and Gelatin) by using separate solution method and fixed interfering mixed method.

The UV-spectrophotometric method which includes:

- The derivative spectra, the first-derivative (^1D) spectra for Chloramphenicol sodium succinate solutions (2-64 mg/L) in wavelength equal 258 nm with (r^2=0.99925). The analytical methods results showed to be simple, rapid and with a good accuracy by comparing between First Derivative (^1D) and direct method of Ion selective electrode by using F-test. The results shown, that the Chloramphenicol sodium succinate can be determined by using Ion selective electrode method because the value of the (F) experimental less than the value of the (F) theoretical at 95% confidence limit. Since $F_{calculated} < F_{table}$, we concluded that there is no significant difference in precision between two methods.

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Abbreviations

CPP	Chloramphenicol palmitate
CPSS	Chloramphenicol sodium succinate
CPSS-Fe(III)	Chloramphenicol sodium succinate- Iron(III)
CST	stock unit of viscosity gm/sec.cm.density
DBP	Dibutylphosphate
DBPH	Dibutylphthalate
DOP	Dioctylphthalate
DS	Derivative spectrophotometry
E	Relative error
e.m.f	Electromotive force
FIM	Fixed interference method
FPM	Fixed primary ion method
FTIR	Fourier transform infrared spectroscopy
F.W.	Formula weight
HPLC	High performance liquid chromatography
ISE	Ion-selective electrode
LC	liquid chromatography
IUPAC	International Union Pure and Applied Chemistry
MPM	Match potential method
MSA	Multi Standard addition method
mV	Millivolt
PVC	Poly vinyl chloride
Re	Recovery
RSD	Relative standard deviation
SAM	Standard addition method
SCE	Saturated calomel electrode
SDI	State company for drug industries
SHE	Standard hydrogen electrode
Std.	Standard
TBP	Tributylphosphate
THF	Tetrahydrofuran
TPB	Sodium tetraphenylborate
TSM	Two solution method
UV	Ultraviolet

Introduction

1-1-Ion-selective electrode (ISE):-

Chemical sensors are miniaturized analytical devices, which can deliver real-time and on-line information on the presence of specific compounds or ions in complex samples. Usually an analyte recognition process takes place followed by the conversion of chemical information into an electrical or optical signal. Among various classes of chemical sensors ion-selective electrodes (ISE) are one of the most frequently used potentiometric sensors during laboratory analysis as well as in industry, process control, physiological measurements, and environmental monitoring. An ion-selective membrane is the key component of all potentiometric ion sensors. It establishes the preference with which the sensor responds to the analyte in the presence of various interfering ions from the sample. If ions can penetrate the boundary between two phases, then an electrochemical equilibrium will be reached, in which different potentials in the two phases are formed. If only one type of an ion can be exchanged between the two phases, then the potential difference formed between the phases is governed only by the activities of this target ion in these phases.[1]

1-2-Design of the electrochemical cell:-

Generally, the cell contains two reference electrodes, “internal” and “external”, and a selective membrane as the recognition element. Conventional notation of the cell is**:**

External ref. / test solution / membrane /internal ref. /internal solution [2]

1-3-Measurments of ion selective electrode cell:-

The operation of ion selective electrodes is based on the fact that there is a linear relationship between the electrical potential developed between an ISE and a reference electrode immersed in the same solution as shown in Figure1-1, and the logarithm of the activity of the ions in the solution. This relationship is described by the Nernst equation:

$$E = E^0 - (2.303RT/ ZF) \log (a) \qquad \ldots.1\text{-}1$$

Where E = the total potential (in mV) developed between the sensing and reference electrodes, E^0 = is a constant which is characteristic of the particular ISE/reference pair, 2.303 = the conversion factor from natural to base10 logarithm, R = the gas constant (8.314 joules/degree/mole), T = the absolute temperature, Z = the charge of the ion, F = the faraday constant (96500 coulombs per mole). log (a) = the logarithm of the activity of the measured ion. [3]

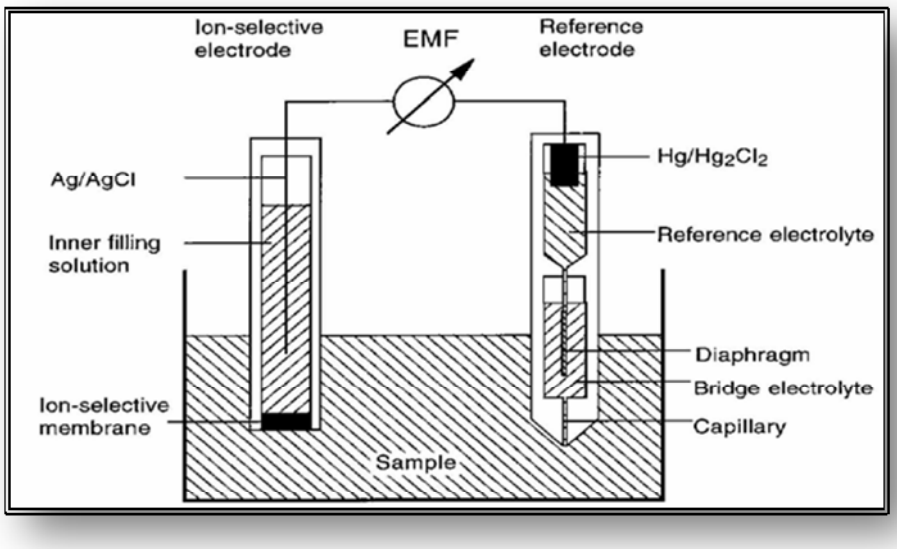


Figure 1-1:- A classical ion –selective electrode in electrochemical cell. [4]

1-4-Classification of membrane electrodes:-[5]

1-4-1- Ion-selective electrodes:-

1-4-1-1- Crystalline Electrodes:- contain mobile ions of one sign and fixed sites of opposite sign. They may be homogeneous or heterogeneous.

-Homogeneous membrane electrodes:- are ion-selective electrodes in which the membrane is a crystalline material prepared from either a single compound or a homogeneous mixture of compounds, for example; the fluoride ISE has a lanthanum trifluoride crystal and mixed crystal such as Ag_2S for Ag^+ or S^{2-} and AgCl for Ag^+ or Cl^- ions [6,7,8].

-Heterogeneous membrane electrodes:- are ion-selective electrodes prepared of an active substance, or mixture of active substances, mixed with an inert matrix (such as silicone rubber or PVC).[6,7,8]

1-4-1-2- ***Non-crystalline Electrodes:-*** In these electrodes, a support matrix, containing an ion exchanger (either cationic or anionic), a plasticizer solvent, and possibly an uncharged, selectivity-enhancing species, form the ion-selective membrane which is usually interposed between two aqueous solutions as shown in Figure1-2 (a), The most common glass electrode is the pH electrode.[9]

- Rigid, self-supporting, matrix electrodes:- ion selective electrodes in which the sensing membrane is a thin polymer with fixed sites or a thin piece of glass, for example (amino-poly (viny1chloride)).[10]

- Electrodes with mobile charged sites:

1. ***Positively charged, hydrophobic cations***:- provide membranes which are sensitive to changes in the activities of anions, for example (quaternary ammonium salts) .[10,11]

2. ***Negatively charged hydrophobic anions:-*** provide membranes which are sensitive to changes in the activities of cations, for example (tetra-phenylborate) .[12]

3. ***Uncharged "carrier" electrodes:-*** provide membrane preparations to give sensitivity and selectivity to certain cations and anions, for example (benzo-15-5 crown ether).[13]

4. ***Hydrophobic ion-pair electrodes***:- containing a dissolved hydrophobic ion pair responds to component ion activities in bathing electrolytes, for example (cationic drug as cation tetraphenylborate or anionic drug as tetra-alkylammonium salt of an anion) .[14]

1-4-2- *Compound or multiple membrane (multilayer) ion-selective electrodes:-*

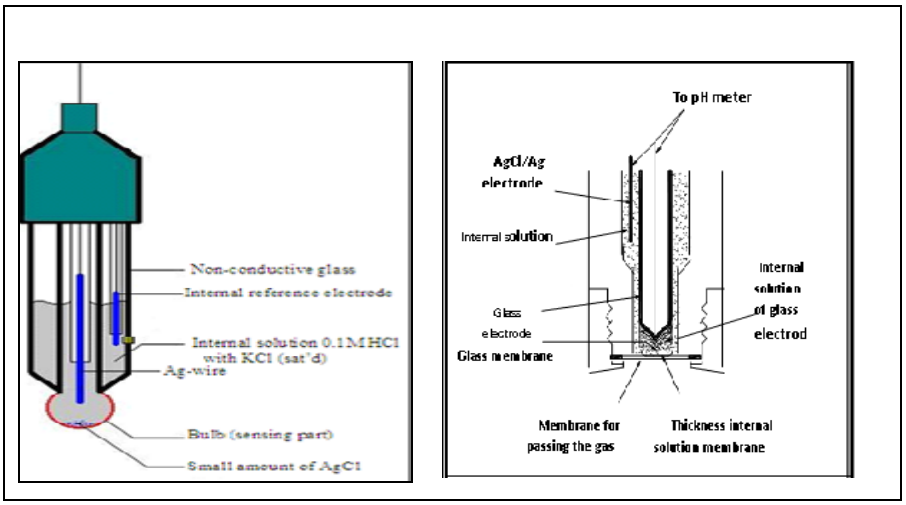
1-4-2-1-Gas sensing electrode:- is a sensor composed of an ion-selective electrode (indicator electrode) and a reference electrode in contact with a thin film of solution which is separated from the bulk of the sample solution by a gas-permeable membrane or an air gap as shown in Figure 1-2 (b), example for (CO_2, NO_2, SO_2) .[15]

1-4-2-2-Enzyme substrate electrode:- is a sensors in which an ion-selective electrode is covered with a coating containing an enzyme which reacts with an organic substance (substrate), such as urease membrane and glucose membrane.[10,16]

1-4-3-Metal contact or all-solid-state ion-selective electrodes:-

There is no inner electrolyte solution in these electrodes, and the charge transfer is accomplished in the membrane by both ionic and electronic conductivities (mixed conductors). The inner reference electrode is replaced

by an electronic conductor, e.g., a bromide sensor film of AgBr is reversibly contacted with Ag, or an anion sensor based on cation radical salts is contacted with Pt. [5]



(a) glass cell *(b) A gas sensing electrodes*

Figure 1-2:- a- A glass cell type [9], b- A gas sensing electrodes type [17].

1-5-Reference electrodes:-

The potential of a reference electrode is determined by the element metal and the active species concentration in the electrolyte. The form of the electrolyte, wet or gelled, has no effect on the reference potential. Both the measuring electrode and the reference electrode are redox half-cell reactions that exist in equilibria.[18] A reference electrode has a stable and well defined electrochemical potential. A good reference electrode is therefore non-polarizable, in other words, the potential of such an electrode will remain stable upon passage of a small current. [3,19]

1-5-1- Types of reference electrodes:-

1-5-1-1- Standard Hydrogen Electrode (SHE):-[20]

An absolute standard for the measurement of electrochemical potentials is not available. It is therefore that the equilibrium potential of the so called

Standard Hydrogen Electrode (SHE) is defined as being 0 Volt at $a(H^+) = 1$ In practice this means that the following reaction:

$$2\,H^+ + 2\,e^- \rightarrow H_2\uparrow$$

The SHE is difficult to use in practice as it involves bubbling H_2 gas through solution.

1-5-1-2-Silver / Silver chloride electrode:- *[21]*

A silver chloride electrode is a type of reference electrode, commonly used in electrochemical measurements. For example, it is usually the internal reference electrode in pH meters as shown in Figure1-3(a), the equation of this electrode can be represented as follows:

$$AgCl + e^- \rightarrow Ag + Cl^-$$

The potential of this electrode is +0.197 Volt vs SHE at 25°C.

1-5-1-3- Saturated Calomel Electrode (SCE) :- *[22]*

The SCE is a half cell composed of mercurous chloride (Hg_2Cl_2, calomel) in contact with a mercury pool. These components are either layered under a saturated solution of potassium chloride (KCl) or within a fritted compartment surrounded by the saturated KCl solution (called double-junction arrangement). A platinum wire is generally used to allow contact to the external circuit as shown in Figure1-3(b), E^0 value of this electrode is +0.244 V. The half reaction is described by:-

$$Hg_2Cl_2 + 2e^- \leftrightarrow 2Hg + 2Cl^-$$

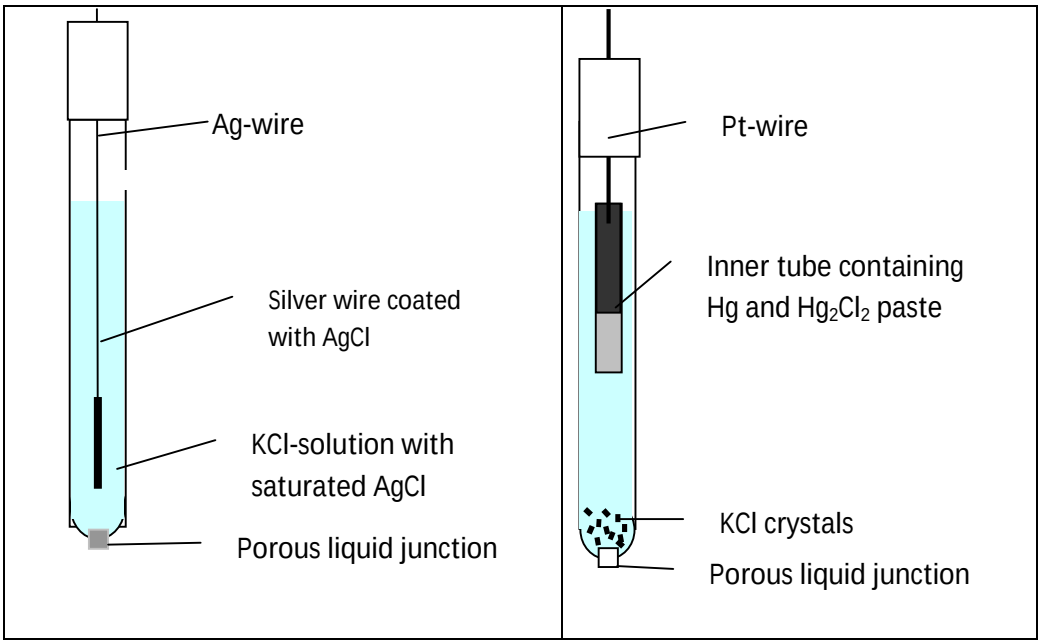
1-5-1-4-Mercury/mercury sulphate Electrode (Hg/Hg_2SO_4 in 0.5M H_2SO_4):- [3,20,23]

This reference electrode is used in some cases where the use of chloride ions is not desirable. The electrode potential of this system is +0.680 Volt vs. SHE .The following reaction is taking place:

$$Hg_2SO_4 + 2\ e^- \rightarrow 2\ Hg + SO_4^{-2}$$

1-5-1-5- Mercury/mercury oxide (Hg/HgO in 1 M NaOH):- [8,24]

It used in alkaline solutions only. The electrode potential of this electrode is +0.140 Volt vs. SHE. The main drawbacks of Hg/HgO reference electrode are difficulties of handling and fabricating of liquid mercury electrode materials.



(a) Silver-silver chloride electrode *(b) Saturated Calomel Electrode*

Figure 1-3:- (a) Ag/AgCl electrode [25] ***, (b) -SCE*** [25]

1-6-Characterization of an ion-selective electrode:-[1]

Ion selective electrode has many properties like:

1-6-1- Calibration curve:-[1,26]

The calibration curve of an ion-selective electrode can be measured and plotted as the signal (electromotive force) versus the log activity of the analyte. Typical calibration curve is shown in Figure 1-4. The linear range of the calibration curve is usually applied to determine the activity of the target ion in any unknown solution. However, it should be pointed out that only at constant ionic strength.

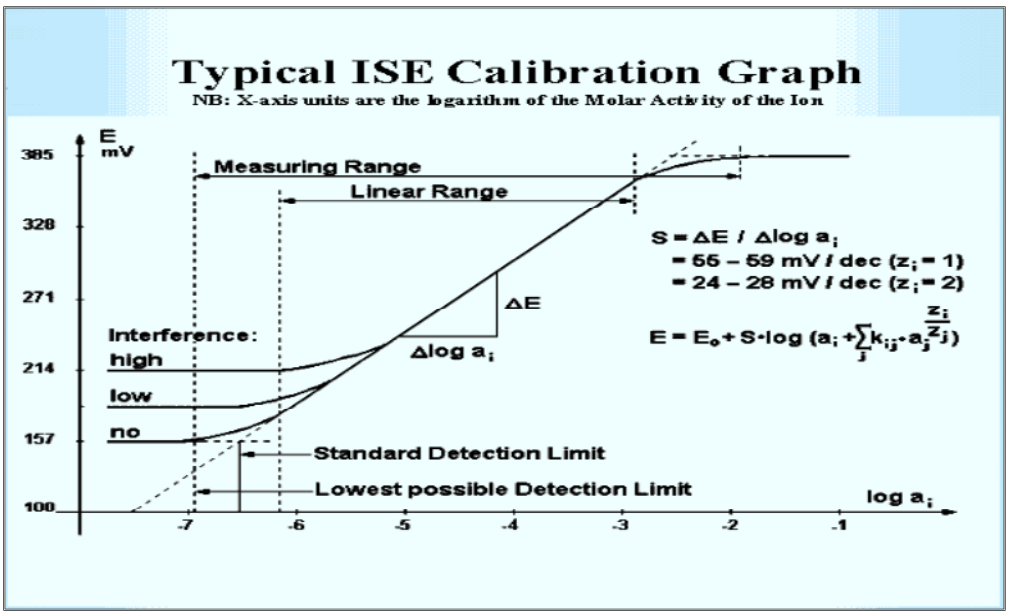


Figure 1-4: Typical ISE calibration graph.[2]

1-6-2- Range of linear response:-[1,4]

At high and very low target ion activities there are deviations from linearity. Typically, the electrode calibration curve exhibits linear response range between 10^{-1}M and 10^{-5}M. As shown in Figure 1-4, through which a

linear regression would demonstrate that the data point does not deviate from linearity by more than ± 2 mV.

1-6-3- Detection limit:-[1,27]

According to the IUPAC recommendation the detection limit is defined by the cross-section of the two extrapolated linear parts of the ion-selective calibration curve as show in Figure1-4. In practice, detection limit on the order of 10^{-5}-10^{-6}M is measured for most of ion-selective electrodes. The observed detection limit is often governed by the presence of other interfering ions or impurities.

1-6-4- Response time:- [1,28]

In earlier IUPAC recommendations, it was defined as the time between the instant at which the ion-selective electrode and a reference electrode are dipped in the sample solution (or the time at which the ion concentration in a solution is changed on contact with ISE and a reference electrode) and the first instant at which the potential of the cell becomes equal to its steady-state value within 1 [mV] or has reached 90% of the final value (in certain cases also 63% or 95%).

1-6-5- Slope:-[1,3,29]

The slope of the linear part of the measured calibration curve, which is the theoretical value according to the Nernst equation is: 59.16/Z [mV/decade] at 298 K and its equal to 59.16, 29.58 and 19.72 for single, double and triple charged ions respectively, and useful can be arranged as (50-60), (25-30), (18-21) respectively. However, in certain applications the

value of the electrode slope is not critical and worse value does not exclude its usefulness.

1-6-6- Stability and Lifetime:- [30]

The stability and lifetime are features associated with the response behavior of ISEs. A number of problems affect the stability and lifetime of PVC based electrodes. They include the same factors which influence the response time (solution concentration, the interfering ions, which poison the electrode surface), and the limited solubility of the active material, and its solvent, which affect the content of the membrane to leak away. All these lead to a positive or negative drift in the response and slope values, indicating that the electrode is approaching the end of its life.

1-6-7- Selectivity:- [1,31]

The selectivity is one of the most important characteristics of an electrode, as it often determines whether a reliable measurement in the sample is possible or not. The selectivity coefficient ($K_{A,B}$) as defined already in the 1960s, offer the best possibility to characterize the selectivity behavior of ISEs. They not only have the best predictive capabilities but they also can be directly related to thermodynamic data of two-phase equilibria. The selectivity coefficient has been introduced in the Nikolski-Eisenman equation which represented as:

$$E = E^0 + R\,T / Z_A F \ln [a_A + \Sigma K_{A,B} (a_B)^{z_A/z_B}] \qquad .....1\text{-}2$$

Most often it is expressed as the logarithm of ($K_{A,B}$). Negative values indicate a preference for the target ion relative to the interfering ion. Positive values of log $K_{A,B}$ indicate the preference of an electrode for the interfering

ion. The experimental selectivity coefficients depend on the activity and a method of their determination. Different methods of the selectivity determination can be found in the literature. The IUPAC suggests two methods: separate solution method (SSM) and mixed solution method (MSM). There is also an alternative method of the selectivity determination called matched potential method (MPM).

1-6-7-1- Separate Solution Methods (SSM):-[32]

1-6-7-1-1-separate solution with equal activity (a_A=a_B):-[33]

The emf of a cell comprising an ion-selective electrode and a reference electrode (ISE cell) is measured for each of two separate solutions, one containing the ion A of the activity a_A (but no B), the other containing the ion B at the same activity a_B=a_A (but no A). If the measured values are E_A and E_B respectively, then the value of $K^{pot}_{A,B}$ may be calculated from the equation:

$$\log K^{pot}_{A,B} = (E_B - E_A)\, Z_A\, F / R\, T \ln 10 + (1 - Z_A/z_B) \log a_A \qquad \ldots 1\text{-}3$$

or for any electrode in general, where (Z_A F/ R T ln10) = 1/S

$$\log K^{pot}_{A,B} = (E_B - E_A)/S + (1 - z_A/z_B) \log a_A \qquad \ldots 1\text{-}4$$

Where (S) is the slope of the electrode. This method is recommended only if the electrode exhibits a Nernstian response. It is less desirable because it does not represent as well the actual conditions under which the electrodes are used.[34]

1-6-7-1-2-separate solution with equal potential (E_A=E_B):-[2,32]

The concentrations of two different solution introduced separately into the cell, a cell comprised of an ion-selective electrode and a reference electrode (ISE cell), are adjusted with each of two different solutions, one

containing the ion A of the activity a_A (but no B), the other containing the ion B (but no A) of the activity a_B as much as required to achieve the same cell potential measured. From any pair of activities a_A and a_B for which the cell potential is the same, the value of $K_{A,B}^{pot}$ may be calculated from the equation:

$$K^{pot}_{A,B} = a_A / (a_B)^{z_A/z_B} \qquad .....1\text{-}5$$

1-6-7-2- Mixed solution methods(MSM):-[35]

1-6-7-2-1- Fixed interference method (FIM):-[35,36,37,38]

The electromotive force (emf) of a cell comprising an ion-selective electrode and a reference electrode (ISE cell) is measured for solutions of constant activity of the interfering ion (a_B) and varying activity of the primary ion (a_A) . The emf values obtained are plotted vs. the logarithm of the activity of the primary ion. The intersection of the extrapolated linear portions of this plot indicates the value of (a_A), as in Figure1-5 is to be used to calculate $K^{pot}_{A,B}$ by using equation 1-5.

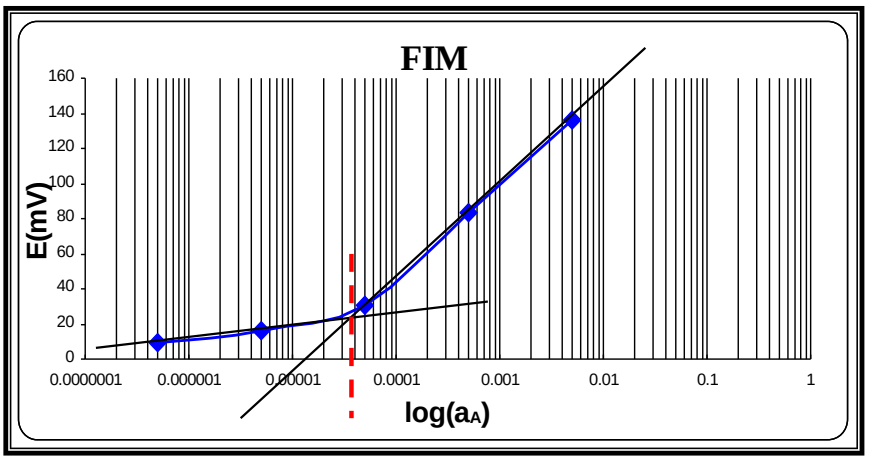


Figure 1-5:-Determination of a_A value according to FIM.

1-6-7-2-2- Fixed primary ion method (FPM):-[35,39]

The emf of a cell comprising an ion-selective electrode and a reference electrode (ISE cell) is measured for solutions of constant activity of the primary ion (a_A) and varying activity of the interfering ion (a_B).

The emf values obtained are plotted vs. the logarithm of the activity of the interfering ion(a_B). The intersection of the extrapolated linear portions of this plot indicates the value of a_B, That is to be used to calculate $K^{pot}_{A,B}$ using equation 1-5.

1-6-7-2-3- Two solution method (TSM):-[35]

This method involves measuring potentials of a pure solution of the primary ion, E_A, and a mixed solution containing the primary and interfering ions, E_{A+B}. The potentiometric selectivity coefficient is calculated by inserting the value of the potential difference, $\Delta E = E_{A+B} - E_A$, into the following equation:

$$K^{pot}_{A,B} = a_A \left(e^{\Delta E\, Z_A\, F / (R\, T)} - 1\right) / (a_B)^{z_A/z_B} \qquad \ldots\ldots 1\text{-}6$$

1-6-7-2-4- Matched potential method (MPM):-[40,41,42]

The $K_{A,B}$ of MPM value is determined as follows: the potential change upon increasing the primary analyte activity by an increment of Δa_A in a starting solution is measured. Interfering ions are then added to an identical starting solution until the same potential change is observed. The selectivity factor $K^{MPM}_{A,B}$ is then obtained as the ratio of the changes in the activity of the analyte, Δa_A and interfering ion Δa_B

$$K^{MPM}_{A,B} = \Delta a_A / \Delta a_B \qquad \ldots. 1\text{-}7$$

With $\Delta a_A = (a_A' - a_A)$

The activity a_A is calculated from the ionic strength of the solution. While the primary ion is added step by step, the potential change is measured and plotted against a_A (curve I_A) in Figure1-6. Another curve, I_{A+B}, is obtained from the potential change by stepwise adding the interfering ion B to the reference solution with the same composition as on curve I_A.

The method is applicable in cases of non- Nernstian responses, although highly discriminated interfering cations sometimes induce negative potential changes that lead to useless selectivity factors. Ordinarily, the sign of a log $K^{MPM}_{A,B}$ value shows whether the ISE responds more strongly to the primary or to the interfering ion at the concentrations at which they were measured.

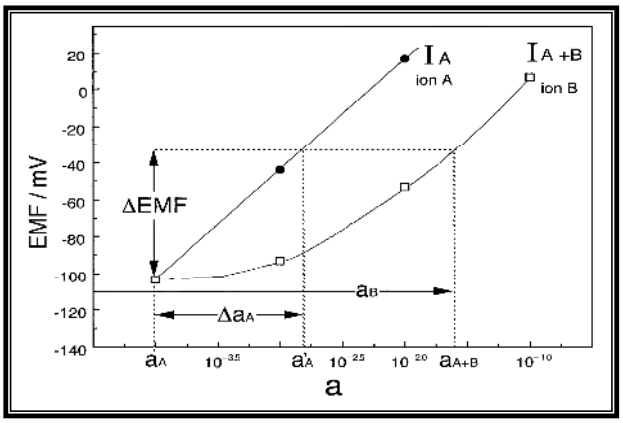


Figure 1-6:-Determination of selectivity coefficients by the MPM. *[43]*

1-7- Methods of analysis:- *[44]*

Potentiometric ion analyses with ISEs are performed by use of one of three methods, each entailing its own advantages: Direct potentiometry, Incremental methods, and Potentiometric titration.

1-7-1- Direct Potentiometry:- *[3,42,44]*

This method is a widely used of performing ion analysis with ISEs. Simply measure the electrode response in an unknown solution and calculate

the concentration directly from the regression line of the calibration curve or manually by using a special type of graph paper called the semi-log (or log/mm) paper is used. Semi-log paper comes in one cycle, two cycles, three cycles…etc. Each cycle is an exact repetition of single cycle. Each single cycle corresponds to an order of magnitude or decade, or by using special computer graphics and calculations (eg. Microsoft Office Excel). A big advantage of this method is that it can be used to measure large batches of samples covering a wide range of concentrations very rapidly without having to change range, recalibrate or make any complicated calculations.

1-7-2- Incremental Methods:-[44]

These methods are useful techniques used to determine ion concentration quickly in samples whose constituents are variable. Incremental methods have some inherent advantages over direct potentiometry. The techniques can reduce errors from variables such as temperature, viscosity, pH or ionic strength. This method involves three types:

1-7-2-1- Standard Addition method (SAM):-[3,28]

This method (also known as "Known Addition") involves adding a small volume of a concentrated standard to a much larger volume of sample. The volume and concentration of the standard must be chosen to cause a significant and measurable change in the concentration of the detected ion (and hence in the measured voltage) but should not cause a significant dilution of the sample matrix (so that the ionic strength remains essentially unchanged). The voltage is first measured in a measured volume of the sample. Then a measured volume of standard is added, the solutions are mixed well and a second reading is taken before calculating the

concentration of the sample. The main advantage of this method is that calibration and sample measurement are both made essentially at the same time and in the same solution. This method follow the equation:

$$\mathbf{C_U = C_S / 10^{\Delta E/S} [1+ (V_U / V_S)] - (V_U / V_S)} \qquad \text{.....1-8}$$

Where C_U, C_S, V_U and V_S are the concentration and volume of unknown and standard solution respectively.

1-7-2-2- Multiple standard addition method (MSA):-[3,30,45]

In this method several addition of standard solution to the same sample to be measured in order to increase the accuracy and decreases the errors. It is an extension of standard method, The response of ion-selective electrode to certain analyte A in solution free from interfering ions can be represented by Nernst equation:-

$$\mathbf{E = E^0 + S \log a_A \times V_S/V_U} \qquad \text{……1-9}$$

Where: S: slope, V_S: volume of added standard, V_U: volume of unknown, V_U is usually set to be hundred times more than V_S. by Rearranging of equation and taking the antilog gives:

$$\mathbf{Antilog\ (E/S) = constant \times a_A\ V_S/V_U} \qquad \text{……1-10}$$

Where antilog (E^0/S) is constant thus the antilog (E/S) is proportional to V_S. A plot of antilog (E/S) against V_S, a straight line is obtained, the intercept of which with the volume axis denote the end point of the unknown concentration in an addition method. The concentration of sample (unknown) can be calculated:

$$\mathbf{C_U} = V_{so} \times \mathbf{C_S / V_U} \qquad \text{…1-11}$$

Where C_U and C_S are the concentration of unknown and standard, respectively, V_{so} is the volume of standard.[46]

1-7-2-3- Potentiometric Titration:-[3,44]

This method can increase the precision of ISE measurements and also the number of ionic species that can be determined. ISEs are commonly used as indicators for the titrant or sample species to follow the progress of a precipitation or complexation titration. A small change in reactant addition corresponds to a large change in electrode potential at the stoichiometric end point. The sample is titrated with a suitable titrant and the increase or decrease in titrant activity is followed with an ion-selective electrode response, to locate the equivalence point. A direct plot of potential as a function of titrant volume, the midpoint in the steeply rising portion of the curve is estimated visually and taken as end point. A second approach to end point detection is to calculate the change in potential per unit volume of titrant $\Delta E/\Delta V$ plotted versus the average volume of titrant, the maximum is the end point.

1-8-Limitation in ISE measurements:- [47,48]

1-8-1-Diffusion:- Orion Research points out that diferences in the rates of diffusion of ions based on size can lead to some error.[49]

1-8-2-Sample Ionic Strength:-[50] Covington points out that the total ionic strength of a sample affects the activity coefficient and that it is important that this factor stay constant. In order accomplish this , the addition of an ionic strength adjuster is used. This adjustment is large, compared to the ionic strength of the sample, such that variation between samples becomes small and the potential for error is reduced.

1-8-3-Temperature:-[47] It is important that temperature be controled as variation in this parameter can lead to significant measurement errors. A single degree (C) change in sample temperature can lead to measurement errors greater than 4%.

1-8-4-pH:-[47] Some samples may require conversion of the analyte to one form by adjusting the pH of the solution (e.g. ammonia). Failure to adjust the pH in these instances can lead to signifiacant measurement errors.

1-8-5-Interferances:-[3] The biggest limitation and difficulty with ion selective electrode measurements is the problem of interference from other ions. ISEs are not ion-specific. All are sensitive to some other ions to some extent. In many cases the interferences are trivial and can be ignored but in some extreme cases the electrode is far more sensitive to the interfering ion than to the primary ion and can only be used if the interfering ion is absent, or only present in very low concentrations relative to the primary ion.

1-9-General Application of ISEs:-[3] ion selective electrodes are used in a wide variety of applications for determining the concentrations of various ions in solutions. Table 1-1 shows some applications of ISEs.

Table 1-1 some applications of ISEs

The application	Examples	References
Explosives	Fluoride, chloride and nitrate have been measured in explosives and their combustion products.	51
Pollution Monitoring	pH of acid rain, soil, surface water, contamination of surface water and ground water with ammonium and nitrate.	52
Agriculture	Soil and fertilizer analysis for Nitrate, Ammonium and Potassium to optimize the use of fertilizer.	53
Food Processing	Nitrate in meat and vegetables.	54
Biomedical Laboratories	ISEs were used to determine important species such as calcium, potassium, sodium and chloride in body fluids (blood, serum, plasma).	55

1-10- Applications of ISEs in pharmaceutical samples:-

ISE has an impressive list of advantages such as being portable, suitable for either direct determination or using as a sensor in titrations besides, these membrane electrode don't affect the studied solutions.[4] Table 1-2 shows some applications of ion selective electrodes in pharmaceuticals.

Table 1-2:-Some applications of ion selective electrodes in pharmaceuticals.

Pharmaceuticals	Membrane components	Linear range(M)	Detection Limit(M)	Slope (mV/decade)	Ref.
Amantadine hydochloride	Amantadine-tetraphenylborate ion pair complex and (DOP) as plasticizer.	10^{-1}-10^{-5}	1.88×10^{-4}	55.5	12
Moroxydine hydrochloride	Moroxydine-tetraphenylborate ion pair complex and (DOP) as plasticizer.	10^{-1}-10^{-5}	2.08×10^{-4}	56.2	12
Trazodone	trazodone-tetraphenylborate ion pair complex and (DBPH) as plasticizer.	5×10^{-5}-1×10^{-2}	1.8×10^{-5}	59.3	56
Fluconazole	fluconazole-tetraphenylborate ion pair complex and (DBPH) as plasticizer.	5×10^{-5}–5×10^{-2}	4×10^{-5}	57.0	57
Sulpiride	sulpiride-tetraphenylborate ion pair complex and (NPOE) as plasticizer.	10^{-4}-10^{-2}	4.2×10^{-5}	58.4	58
Methacycline Hydrochloride	Methacycline-tetraphenylborate as the electroactive substance and (DOP) as plasticizing.	3×10^{-2}-6×10^{-6}	3.4×10^{-6}	52.9	59
Sibutramine hydrochloride	Sibutramine- tetraphenylborate ion pair complex and (DBP) as plasticizer.	3.8×10^{-5}-1×10^{-2}	8.9x 10^{-6}	57.7	60
Clozapine	Clozapine-phosphotungstate ion pair complex by use dioctyl sebacate as plasticizer.	1×10^{-5}–1×10^{-2}	3.7 x 10^{-6}	57.4	61
Bromazepam	Bromazepam-phosphotungestiate ion pair complex and (ONPOE) as plasticizer	10^{-2} -10^{-4}	3×10^{-5}	52.0	62
Methylene blue	Methylene -phosphotungstate ion pair and (DBPH)as plasticizer.	10^{-3} -10^{-6}	6.79×10^{-7}	51.5	63
Atenolol	Atenolol-phosphotungstate as an active material by used (DOP) as plasticizer.	3×10^{-4}-5×10^{-2}	5×10^{-5}	55.9	64
Ampicillin	$(Ampicillin)_3$ phosphotungstic acid ion pair with poly vinyl chloride.	1×10^{-1}-2.5×10^{-3}	1×10^{-4}	59	65
Amiloride	Amiloride- phosphotungstic acid ion pair complex and (DBPH) as plasticizer.	10^{-5}–10^{-2}	6×10^{-7}	54.1	66
Amoxicillin	Amoxicillin-phosphotungestate ion pair complex and (DBP) as plasticizer.	5×10^{-6}-10^{-2}	2×10^{-6}	58.7	67
Cephalexin	Cephalexin-phosphotungestate ion pair complex and (DBPH) as plasticizer.	10^{-4}-10^{-2}	5×10^{-5}	59.5	68

Pharmaceuticals	Membrane components	Linear range(M)	Detection Limit(M)	Slope (mV/decade)	Ref.
Ramipril	Ramipril- molybdophosphoric acid ion pair complex and (DOP) as plasticizer.	10^{-2}-10^{-5}	3×10^{-6}	53	69
Gabapentin	gabapentin - molybdophosphoric acid ion pair complex and (DOP) as plasticizer.	1×10^{-5} -5×10^{-2}	1×10^{-5}	59.8	70
Tramadol Hydrochloride	Tramadol- molybdophosphoric acid ion pair complex and (DBP) as plasticizer.	2×10^{-6} -1×10^{-1}	1.3×10^{-6}	58.3	71
Dothiepin hydrochloride	Dothiepin -tungstosilicic acid ion pair complex and Bis(2-ethylhexyl sebactate) as plasticizer.	10^{-1} -10^{-4}	2×10^{-3}	55	72

1-11- Spectrophotometric method:-

Photometric methods whether UV, visible, or FTIR, are characterized by their sensitivity and selectivity. UV-visible regions are usually of greater practical application of drugs because the molar absorptivity exhibited are usually of high order of magnitude than those in the FTIR. Thus greater sensitivity can be obtained at these spectra region [73]. The wavelength range of ultraviolet (UV) radiation starts from 200 nm and ends to 400 nm. The radiation of UV has sufficient energy to excite valance electrons in many atoms or molecules from their ground state to higher energy levels. The excited electrons transfer from a bonding to an anti bonding orbital [74]. Wide applications of UV/Visible spectroscopy include numbers of inorganic metals, organic compounds, and biochemical species absorbed ultraviolet or visible radiation and are thus amenable to direct quantitative determination[75].

1-12 Derivative spectrophotometric analysis:-

1-12-1- Basic Characteristics of Derivative Spectrophotometry:- [76]

-Derivative Spectrophotometry (DS), Derivation.[76]

-Enhancement of the Detectability of Minor Spectral Features.[76]

-Precise Determination of the Positions of Absorption Maxima.[76]

-Increase of Spectra Resolution.[77]

-Elimination of the Influence of Baseline Shift and Matrix Interferences.[77]

-Signal to Noise Ratio (SNR).[78]

1-12-2- Applications of Derivative Spectrophotometry (DS):-

Derivative spectrophotometry (DS) is widely applied in inorganic and organic analysis, toxicology, and clinical analysis, analysis of pharmaceutical products, amino acids and proteins, in analysis of food and in environmental chemistry. In general, the application of DS is not limited to any particular case or filed, but it can be used whenever quantitative or qualitative investigations of broad spectra are difficult.[79]

1-13-The drugs:-

1-13-1- Chloramphenicol palmitate (CPP):-

Chloramphenicol palmitate , $C_{27}H_{42}Cl_2N_2O_6$, the structural formula as shown in Figure 1-7, 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.[80]

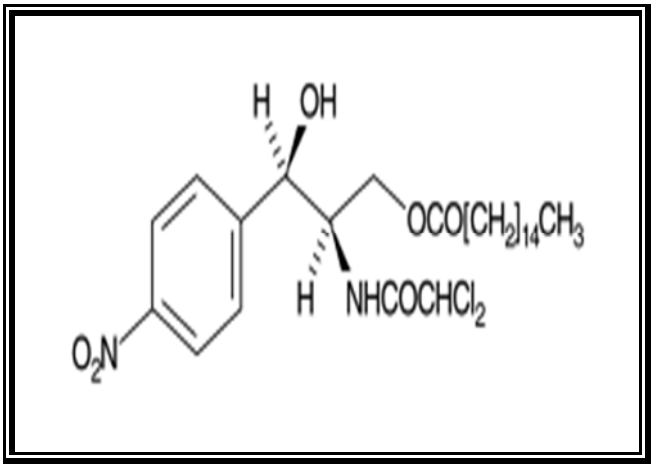


Figure 1-7:-structure formula of chloramphenicol palmitate

Chloramphenicol is a large spectrum antibiotic with antimicrobial activity. Its mechanism of action is based on the inhibition of protein synthesis; Chloramphenicol is available for oral administration as chloramphenicol palmitate - a prodrug of chloramphenicol - developed with the objective of a more pleasent flavored derivative. Chloramphenicol palmitate is quickly and almost completely hydrolyzed by intestinal esterase, being distributed widely throughout corporal liquids and quickly achieving therapeutic levels.[81]

1-13-2- Chloramphenicol sodium succinate (CPSS):-

Chloramphenicol sodium succinate, a white or yellowish-white powder, hygroscopic, very soluble in water, freely soluble in alcohol, practically insoluble in ether. chloramphenicol sodium has a molecular weight of 445.2 .It's empirical formula is $C_{15}H_{15}Cl_2N_2$ NaO_8 and it's structural formula as show in Figure1-8.[82]

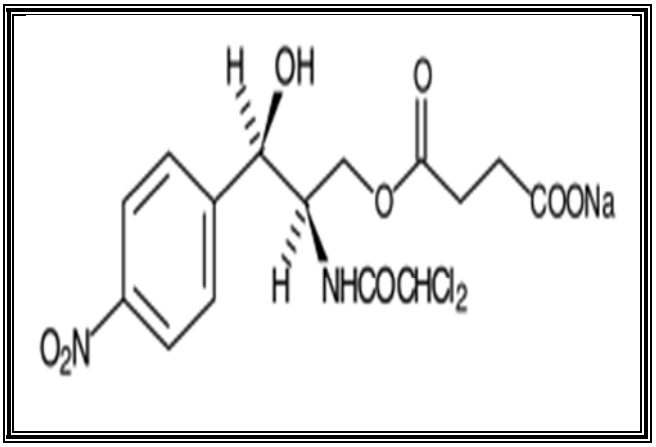


Figure 1-8:-structure formula of chloramphenicol sodium succinate

Chloramphenicol sodium succinate powder for injection should be stored at temperatures less than 40°, and preferably between 15-30°C.[83]

Chloramphenicol may be chosen to initiate antibiotic therapy on the clinical impression that one of the conditions below is believed to be present; in vitro sensitivity tests should be performed concurrently so that the drug may be discontinued as soon as possible if less potentially dangerous agents are indicated by such tests.[84] Chloramphenicol Sodium Succinate injection is used to treat serious infections including bacterial meningitis, typhoid fever, eye infections. Chloramphenicol sodium Succinate belongs to a group of medicines called antibiotics. It works by stopping the growth of bacteria causing your infection.[85] Chloramphenicol sodium succinate for injection must be hydrolyzed to its microbiologically active form, and there is a lag in achieving adequate blood levels compared with the base given intravenously.[86]

1-13-2-1-Analyses of Chloramphenicol sodium succinate:-

There are several methods for analyses chloramphenicol sodium succinate, Table1-3, shows some of these methods.

Table 1-3:- shows some methods for analyses of chloramphenicol sodium succinate.

Method	Notes	Description	Ref.
1-spectrophotometric method	Ninhydrin in the presence of $SnCl_2$ in 0.2M citrate buffer (pH 5) is proposed as a new reagent for the Spectrophotometric assay of (CPSS) in injection.	The resulting violet colour exhibits maximum absorption at 570 nm.	87
Liguid chromatography (LC)	1-Analysis of chloramphenicol and it's succinate in 10µL samples of plasma. A mixture of acetic acid solution (PH3) / acetonitrile(75/25) was used as mobile phase. Separate the compounds in C_{18} cartridge with a radial compression separation system.	Total analysis time for each sample was‹8 min, at a flow rate of 4mL/min.	88
	2-High-performance liquid chromatography was used to assay CPSS and chloramphenicol CP in serum and urine.	Recovery of CPSS in the urine Between 6.5% and 43.5% of the CPSS dose was recovered in the urine of 6 patients.	89
	3-A method for the determination of chloramphenicol and its monosuccinate ester in piglet plasma. It involves precipitation of plasma proteins by addition of methanol to the plasma sample.	Using RP-18 column and phosphate buffer pH 4.9 containing 30% methanol as eluent.a precision of 2.6% and 2.4%	90

1-14-Iron

Iron is a naturally occurring magnet metal that attracts iron and steel. Its chemical symbol is (Fe) atomic weight 55.845 g/mole. Iron is one of the

most common elements found in the earth's crust. It can be found in soils, sediments, water and in most living organisms. Iron is removed from the earth in the form of ores, which are processed and refined to obtain high-grade iron. Most iron ores are used in making iron and steel. These materials are used for building bridges, roads, ships and buildings. Iron is also used in dyes, water treatment, pigments for rubber and paints, and integrated circuits. It is also used as vitamins and supplements.[91]

1-14-1- Iron compounds:-

Iron forms compounds mainly in the +2 and +3 oxidation states for example: iron(II) sulfate ($FeSO_4 \cdot 7H_2O$) and iron(III) chloride ($FeCl_3$) which produced on the largest scale in industry. Iron also occurs in higher oxidation states, an example being the purple potassium ferrate (K_2FeO_4) which contains iron in its +6 oxidation state. There are also many mixed valence compounds that contain both iron(II) and iron(III) centers, such as magnetite and Prussian blue ($Fe_4(Fe[CN]_6)_3$). Iron (II) compounds tend to be oxidized to iron(III) compounds in the air. Iron reacts with oxygen in the air to form various oxide and hydroxide compounds; the most common are iron (II,III) oxide (Fe_3O_4), and iron(III) oxide (Fe_2O_3). The best known compounds of iron are ferric sulfate [92] [$Fe_2(SO_4)_3.9H_2O$] and iron pyrite (FeS_2), also known as fool's gold owing to its golden luster.[93]

1-14-2- Analyses of iron and it's compounds:-

Table 1-4 study some the method which used for analyses of iron and it's compounds.

Table1-4:-shows some methods for analyses iron and it's compounds.

Method	Notes	Description	Ref.
Ion-Selective Electrodes	1-ion-pair formed between $[Fe(citrate)_2]^{3-}$ and the tricaprylylmethylammonium cation in (PVC) matrix pair and dibutylphthalate (DBPH).	Linear range from 1.0 x 10^{-3} mol/L to 1.0 x 10^{-1} mol/L with a slope of 19.3 mV/decade and a useful lifetime of at least six months.The detection limit was 7.5 x 10^{-4} mol/L .	94
	2-The membrane contain DBTS :NaTPB:NB:PVC in the ratio 2:2:64:32 for monitoring Fe^{+3}.	Linear range of 1.0 x $10^{-6}$to 1.0x10^{-2}M with a slope of 19.4 mV per decade. The lower limit of detection was 3.6x 10^{-7} M.	95
	3-Fe^{+3}- aluminum tungestate ion pair complex and dibutylphosphate as plasticizer. the composition AT: PVC: DBP in the ratio 2 : 20 : 15	response time (15 s), concentration range of Fe(III) ions from 1×10^{-7} M to 1×10^{-1} M with a slope of 20 mV per decade, low detection limit, wide working pH range (1–3▫5).	96
spectrophotometric method	1- The hydrolysis of iron(III) was studied in acid aqueous solutions between 25 and 200 °C at saturated water vapour pressure by uv–vis spectrophotometry using a high-temperature, flow-through gold-lined optical cell	At wavelengths below 400 nm, concentrations ranged from 6.184×10^{-5} to 1.652×10^{-4} mol kg^{-1}.	97
	2-Determination of iron(III) and iron(II) and total iron, use mini-column before spectrophotometric detection with 1,10-phenathroline in citrate buffer.	At pH 5.0. The mid-range precision is < 1.4%, at a sampling rate of 60 h^{-1}.	98
Atomic absorption spectrophotometry	The objective of the present study was to perform full validation assays of hepatic iron quantification by atomic absorption spectrophotometry.	A good linear correlation was found (0.9948),Limit of detection was 2 ppb and conc. range (20 -120)ppb.	99
visible spectrophotometry	Determination of frusemide in bulk drug and formulations, is based on redox reaction involving complexation reaction and uses iron(III) and frusemide as reagents.	The resulting Prussian is measured at 760nm and conc. range 0.4-4.0µg mL^{-1}	100
Reflectance spectroscopy	Using ferrihydrite- bearing and ferric sulfate-bearing montmorillonites prepared with variable Fe^{+3} and variable pH conditions.	An absorption minimum is observed at 0.88-0.89µm in spectra of ferric sulfate-bearing samples, and at 0.89-0.92µm for ferrihydrate.	101

Method	Notes	Description	Ref.
first-derivative spectrophotometry	Determination of iron(III) in alloys, The method is based on the formation of the binary complex of iron with Alizarin yellow R (AYR) 5-[4-nitrophenylazo]salicylic acid .	Conc.range1.1–8.3 µg/ml, The detection limits was 2.8 ng/ml for iron, relative standard deviation less than 1.5% .	102
second derivative spectrophotometry	A new reagent ,2-Ketobutyric acid thiosemicarbazone has been used for determination iron(II).	Yellowish-green complex at pH 6.5,absorbance at440nm,conc.range 0.20-2.280µg mL^{-1}	103
third –derivative solid- phase spectrophotometry	microdetermination of iron at sub-mg/L level, (2,4,6-tripyridyl-1,3,5 triazine)used to form blue complex	Signal at 622.0, quantitative determination of iron (0.195–120 $ngmL^{-1}$) and RSD=1.8%.	104
HPLC method	Using a mobile phase consisting of acetonitrile- 0.1% orthophosphoric acid	Linear range was 1.01-121.8µgmL^{-1},detection limit was 0.3 µgmL^{-1}	100

1-15-Aim of the work:-

This project was aimed to construct and characterize two types of ion-selective electrodes for the potentiometric determination of (a) chloramphenicol sodium succinate in pure and pharmaceuticals and (b) Fe(III) which based on chloramphenicol sodium succinate in pure and pharmaceuticals. These electrodes utilize plasticizers as the solvent mediators such as; di-butylphthalate (DBPH), di-butylphosphate (DBP), di-octyl phthalate (DOP), tri-butyl phosphate (TBP). The constructed electrodes characteristic parameters that include slope, linear range, detection limit, lifetime, selectivity, and working pH range will be investigated. Also, the statistical treatments were applied for the results that include: relative standard deviation (RSD%), relative error percent (E_r%), recovery percent (Re%) and confidence limit for concentration .

Several ion selective electrodes for the potentiometric determination of chloramphenicol sodium succinate were constructed by using chloramphenicol palmitate, sodium tetraphenylborate as additive with many plasticizers. Potentiometric measurements including direct method, standard additions method and titration method will be studied. The results of the first-derivative (^{1}D) spectra were compared with chloramphenicol sodium succinate electrodes results by using F-test statistics.

Several ion selective electrodes for the potentiometric determination of Fe(III) were constructed by using [CPSS-Fe(III)] complex with the same plasticizers as above.

2- Experimental part

2-1-Instruments and equipment:-

1-Expandable ion analyzer, Orion, model EA 940, (U. S. A.).

2-Reference electrode single junction, Orion, *(Saturated Calomel Electrode)* model 90-01.

3- Combined glass electrode Orion no.91-02, (swiss made), for measuring pH.

4- Silver-silver chloride wire.

5- Clear PVC tubing (6 mm o.d.).

6- Magnetic stirrer

7- FTIR-8300 fourier transforms infrared spectrophotometer (Shimadzu Japan).

8- Double-beam UV-Visible spectrophotometer model (UV-1650 PC), (Shimadzu Japan), interfaced with computer via a Shimadzu UV probe data system program (Version 1.10).

9- Ultra sonic devise (ultrasonicator) for dissolving samples, (W. Germany).

2-2-Chemicals:-

1-The chemical compounds were used throughout the study, their molecular formulas, formula weights and purity are tabulated in Table 2-1.

Table 2-1: Shows types of used chemicals compounds

No.	Component name	Molecular formula	Formula Weight(g/mol)	Purity	Company
1	Chloramphenicol palmitate (CPP)	$C_{27}H_{42}CI_2N_2O_6$	561.6	100%	SDI-IRAQ
2	Chloramphenicol sodium succinate(CPSS)	$C_{15}H_{15}Cl_2N_2\ NaO_8$	445.2	100%	SDI-IRAQ
3	Folic acid	$C_{19}H_{19}N_7O_6$	441.4	100%	SDI-IRAQ
4	Ferric (III) sulfate	$Fe_2\ (SO_4)_3.9H_2O$	562	99%	Fluka
5	Sodium tetraphenylborate (TPB)	$C_{24}H_{20}BNa$	342.22	98%	BDH
6	Tetrahydrofuran (THF)	C_4H_8O	72	99.5%	Fluka
7	Polyvinyl chloride (PVC)	$((CH_2\text{-}CHCl)_2)_n$	-----	99.5%	Fluka
8	Hydrochloric acid	HCl	36.45	36%	Fluka
9	Sodium hydroxide	NaOH	40.00	98%	BDH

2-Commercial drugs: Chloramphenicol sodium succinate injection (1.00g) equivalent to chloramphenicol, made in (Humberg-Germany). Feroglobin capsules(24 mg iron+12mg zinc+2000µg copper+500µg folic acid), made in (London- England).

3- Other chemicals :-potassium hydrogen phthalate ($C_8H_5KO_4$; F.W.204.22), potassium chloride (KCl; F.W. 74.58), sodium chloride (NaCl; F.W. 58.45), copper (II) sulfate, anhydrous ($CuSO_4$; F.W. 159.60), manganese (II) sulfate, anhydrous ($MnSO_4$; F.W. 151), zinc(II) sulfate, anhydrous ($ZnSO_4$; F.W. 161.36),aluminum (III) chloride ($AlCl_3.6H_2O$; F.W. 241.50), sucrose; ($C_{12}H_{22}O_{11}$; F.W. 342.30) and gelatin; (F.W. 300.0). All chemicals and solvents were of an analytical reagent grade obtained from BDH and Fluka companies, distilled water was used throughout the study.

4-The plasticizers were obtained from Fluka AG, (Switzerland), their composition; purity and viscosity are tabulated in Table 2-2.

Table 2-2:- Shows types of used plasticizers.

No.	Plasticizer's name	Molecular formula	viscosity	Purity	company
1	Di-butylphosphate (DBP)	$(C_8H_{19}O_4)$ P	1I2.88 CST	98.9%	Fluka
2	Di-butylphthalate (DBPH)	$C_6H_4[CO_2CH_3(CH_2)_3]_2$	14.44 CST	99%	Fluka
3	Di-octylphthalate (DOP)	$C_6H_4[CO_2C_8H_{17}]_2$	82.98 CST	98%	Fluka
4	Tri-butylphosphate (TBP)	$(C_4H_7O)_3PO$	3.114 CST	97%	Fluka

2-3-Preparation of standard solutions:-

2-3-1-Standard solutions for ISE:-

1- A stock solution of 0.1 M chloramphenicol sodium succinate was prepared by dissolving 2.226 g of pure chloramphenicol sodium succinate in distilled water and completing the solution up to 50 mL. The other

chloramphenicol sodium succinate standard solutions were prepared by subsequent dilution of the stock solution.

2- A stock solution of 0.01 M of iron(III) solution was prepared by dissolving 0.5031 g of ferric sulfate [$Fe_2(SO_4)_3.9H_2O$] in distilled water with heating until dissolve completely and completing the solution up to 50 mL. The other iron(III) standard solutions were prepared by subsequent dilution of the stock solution ranged (10^{-2}–10^{-7}M).

3- ≈0.1 M of HCl solution was prepared by diluting 1 mL of 12 M HCl up 100 mL by distilled water, and ≈0.1 M of NaOH solution was prepared by weighting 0.4 g of NaOH and dissolving it in 100 mL by distilled water. These two solutions were used for adjusting the pH of solutions. Standard solution of 0.1M potassium hydrogen phthalate was prepared by weighting 2.04g of $C_8H_5KO_4$ and dissolving it in 100 mL of distilled water, and used for standardized of NaOH.

4- Stock solutions of 0.1 M of NaCl, KCl, $CuSO_4$, $MnSO_4$, $ZnSO_4$, $AlCl_3.6H_2O$, sucrose, gelatin ,chloramphenicol palmitate and folic acid were prepared by weighted (0.2922, 0.3729, 0.7980, 0.7550, 0.806, 1.2075, 1.7115, 1.50, 2.8077 and 2.207g) respectively and dissolved by distilled water in 50 mL volumetric flask. More diluted solutions were prepared by dilution from the stock solutions as required.

2-4-Preparation chloramphenicol sodium succinate electrodes:-

Four (CPSS) ion-selective electrodes were prepared depending on the use of chloramphenicol palmitate (CPP) and sodium tetraphenylborate (TPB) as additive with four plasticizers. The method of immobilization the compounds into the PVC matrix membrane was made as described by Mahajan et al [105]. 0.040 g of CPP and 0.040 g of (TPB) were mixed with

0.360 g of plasticizer and 0.17 g of PVC powder; all were dissolved in 5 mL of THF with stirring until a clear viscous solution was obtained. Then CPSS electrodes prepared by the steps as shown in Figure 2-1.

2-5-Assembling the ion-selective electrode:-

The ISE membrane nature and characteristics are considerably influenced by the nature and the amount of each component in its composition. As far as the polymeric membrane is concerned, it separates the test solution from the inner compartment, containing the target ion solution.[106,107]

Figure 2-1 shows the known process for preparation ion selective electrodes.[108]

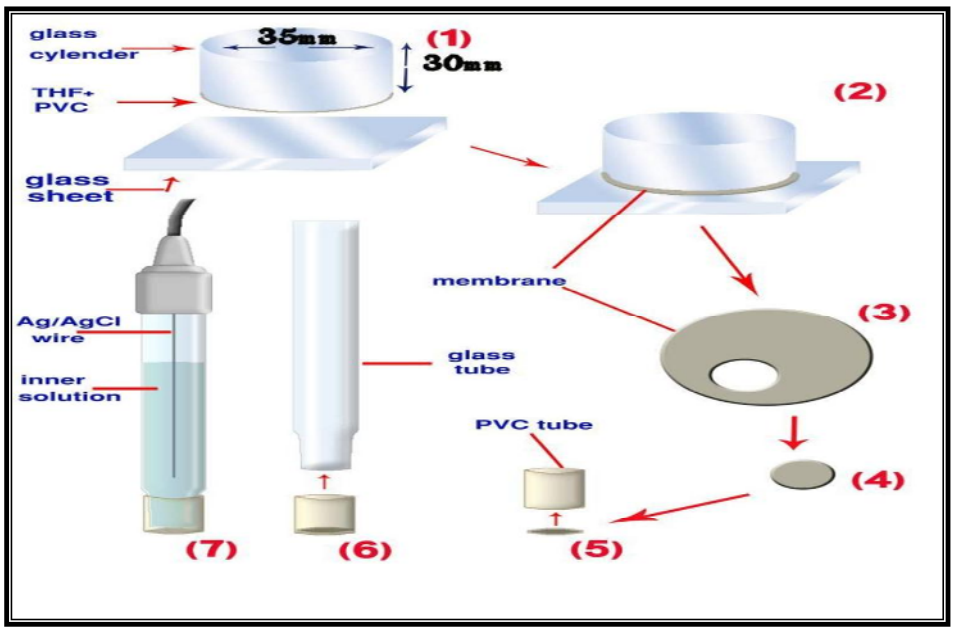


Figure 2-1:- Assembling the ion selective electrode.

2-6-Preparation of ion-pair compound for iron(III) electrodes:-

The preparation of ion-pair complex for [CPSS-Fe(III)] was performed by mixing 30 mL of 0.01 M solution of chloramphenicol sodium succinate (CPSS) with 10 mL of 0.01 M iron(III) with stirring. The resulting deep

yellow precipitate was filtered off, washed with water, dried at room temperature for two days. The composition of the ion-pair compound [CPSS-Fe(III)] was confirmed using FTIR .

2-7-Preparation of iron(III) electrodes:-

The iron (III) ion selective electrodes were constructed using the method given by Craggs et al[109]. A 0.040 g of [CPSS-Fe(III)] ion pair was mixed with 0.360 g of plasticizer and 0.17 g of PVC powder; all were dissolved in 5 mL of THF with stirring until a clear viscous solution was obtained. The iron(III) electrodes was the constructed as described in the steps as shown in Figure 2-1.

2-8-Potential measurement:-

The potentiometric cell was arranged by immersing the ion selective electrode and reference electrode (saturated calomel) in a beaker (50 ml) containing 25mL of analyte standard solutions. The cell was equipped with a magnetic stirrer. The potential measurements were carried out at room temperature. A calibration curve was constructed for each electrode using standard analyte solutions ranged from (10^{-1}-10^{-7} M) for CPSS electrodes and from (10^{-2}-10^{-7} M) for iron(III) electrodes. The calibration curves were prepared by plotting the potential (E) versus the logarithm of analyte concentration by using a computer program (Microsoft office Excel). From the calibration curve, characterization parameters of each ISE were obtained, including; concentration range; slope and detection limit.

The effect of pH on the response of membrane was examined by measuring the potential of the standard solutions of concentrations (10^{-4} , 10^{-3}, 10^{-2} M) at different pH ranged from 0.5 to 11; obtained by addition of small volumes of ≈0.1M hydrochloric acid and/or sodium hydroxide solutions.

The lifetime of each membrane was calculated, when a positive or negative drift in the slope is observed, indicating that the electrode is approaching the lifetime.

2-9-Selectivity measurements:-[1,31]

The influence of some inorganic cations (Na^+, K^+, Mn^{2+}, Cu^{2+}, Zn^{2+}, Fe^{3+} and Al^{3+}) in addition to chloramphenicol palmitate, folic acid, sucrose and gelatein. The selectivity of the ion selective electrodes were studied and the selectivity coefficients were determined by:-

2-9-1-The separate solution methods:-[32,33]

In this method, a 25 mL of $1x10^{-3}$ M solution of the analyte (A) (chloramphenicol sodium succinate or iron(III)) and 25 mL of $1x10^{-3}$ M of each other interfering species (B) (Na^+, K^+, Mn^{2+}, Cu^{2+}, Fe^{3+}, Al^{3+}, chloramphenicol palmitate, sucrose and gelatein) for chloramphenicol sodium succinate electrodes and (Na^+, K^+, Mn^{2+}, Cu^{2+}, Zn^{2+}, Al^{3+} and folic acid) for iron(III) electrodes. The potential of each solution is measured separately. The selectivity coefficient was calculated according to equation 1-4.

2-9-2-Mixed solution methods [fixed interference method (FIM)]:-[35,36,37]

In this method, a 10 mL of analyte (A) solution (chloramphenicol sodium succinate) in concentration range 10^{-7} to 10^{-1} M or (iron(III)) in concentration range 10^{-7} to 10^{-2} M is mixed with 10 mL of 0.1 M of the interfering ion (B) in 50 mL beaker. The potential was measured for each solution. The logarithm of activities of analyte (A) are found after mixing and plotted against the measured potential as shown in Figure 1-5. The values of selectivity coefficient ($K^{pot}_{A,B}$) are calculated according to equation 1-5. The activities of interfering ion (a_B) are calculated after dilution:-

a_B = (0.1 M× 10 mL)/ 20 mL = 5×10^{-2} M.

2-10-Sample analyses:-[44]

2-10-1-Direct method:-[3,44]

Potentiometric measurements of the analyte (A) solutions (chloramphenicol sodium succinate or iron(III)) were carried out directly using the constructed indicator electrodes. The concentration was then calculated using the calibration curve for the standard analyte (A).

2-10-2-Incremental methods:-

2-10-2-1-Standard additions method (SAM):-[3,28]

In this method, the sample of 20 mL with concentration of $1x10^{-3}$ M is introduced into the potentiometric cell, followed by addition of 0.5 mL of 0.01 M increment of analyte (A) solution (chloramphenicol sodium succinate or iron(III)). The potential was measured before and after addition. The concentration of the sample is calculated using equation 1-8 for a single point increment.

2-10-2-2-Multiple standard additions method:-[3,30,45]

This method is an extension of standard additions method, the sample of 20 mL of $1x10^{-3}$ M is introduced into the potentiometric cell followed by addition of 0.5 mL of 0.01 M of analyte (A) solution (chloramphenicol sodium succinate or iron(III)). The potential is recorded before and after each addition. The multi additions method is constructed by plotting the antilog (E/S) against the added volume of standard solution.

2-10-3-Potentiometric titration method:-[3,44]

A precipitation titration was performed for the (CPSS) sample under study. In this method, a 15 mL sample solution containing (CPSS) 0.01 M

was titrated against 0.01 M (TPB) solution. Potential was measured after each addition using the prepared electrode. The midpoint in the steeply rising portion of the curve, resulted from the direct plot of the measured potential as a function of the titrant volume, is estimated visually and taken as an end point. A second approach to end point detection is to calculate the change in potential per unit volume of titrant $\Delta E/\Delta V$ plotted versus the average volume of titrant (first derivative plot), the maximum is the end point.

The same procedure was performed for the iron(III) sample. When a 15 mL sample solution containing iron(III) solution 0.01 M was titrated against 0.1M sodium hydroxide solution.

2-11-Preparation of pharmaceutical formulation:-

All contents of ten vials were mixed (chloramphenicol sodium succinate 1.00g) and dissolved in 1L , the resultant concentration of the prepared solution is equal to 2.24×10^{-2} M. CPSS at concentration 10^{-3}M was prepared by diluting 2.23ml of the stock solution to 50 mL with distilled water.

The content of ten feroglobin capsules were mixed and weighted accurately. The weight average was equal to 0.4257 g per capsule is then dissolved and diluted to 1L with distilled water, the resultant concentration of iron(III) is equal to 4.3×10^{-4} M. Fe(III) solution at concentration 10^{-3}M was prepared by diluting 5.7ml of 4.3×10^{-4} M to 50 mL with distilled water.

2-12-Spectrophotometric Studies:-

2-12-1-Standard solution for chloramphenicol sodium succinate:-

Stock standard solution of 200 mg/L CPSS was prepared by dissolving 0.02 g in 100 mL of distilled water . 10 mL of standard solutions ranged from 2-64 mg/L were prepared by diluting (0.1, 0.2, 0.3, 0.4, 0.5, 1.2, 1.7, 2.2, 2.7 and 3.2) mL with distilled water.

2-12-2-FTIR absorption spectra for [CPSS-Fe(III)]complex :-

FTIR spectra in the range (4000-400) cm^{-1} were recorded using potassium bromide disk with [CPSS-Fe(III)] complex.

3-Results and Discussion

3-1-chloramphenicol sodium succinate electrodes:-

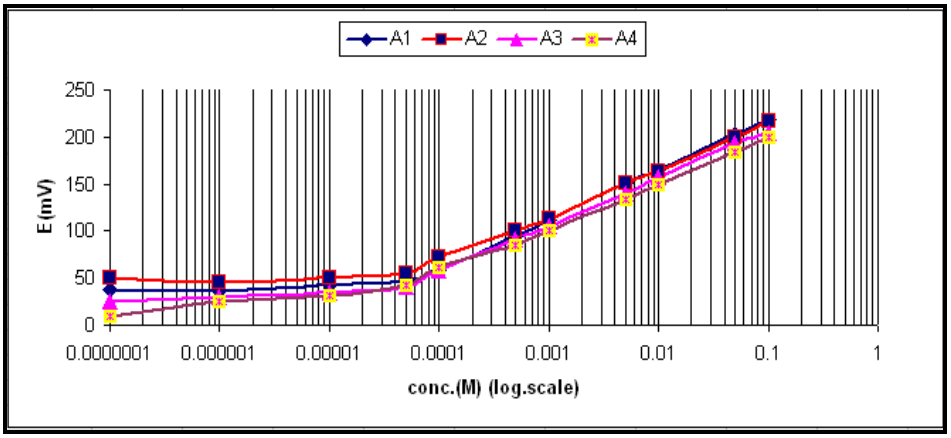
3-1-1- Sensor Characteristics:-

Four electrodes of chloramphenicol sodium succinate (CPSS) (A1, A2, A3, A4) based on using chloramphenicol palmitate (CPP) and tetraphenylborate (TPB) as additive with four plasticizers: Di-butyl phthalate (DBPH); Di-butyl phosphate (DBP); Di-octyl phthalate (DOP); Tri-butyl phosphate (TBP); in PVC matrix were examined respectively. The effects of different plasticizers were studied with respect to the linear concentration range, slope, detection limit, response time and lifetime of the electrode. The measured potential values with these electrodes were plotted versus the logarithm of the drug concentration. All membranes were initially soaked in $1x10^{-1}$ M (CPSS) solution for one hour for condition of the membrane. The calibration curves with (A1, A2, A3 and A4) are shown in Figure 3-1-(a),(b) and (c).These electrodes gave linear ranges from ($1x10^{-4}$-$1x10^{-1}$, $5x10^{-4}$-$1x10^{-1}$, $1x10^{-4}$-$1x10^{-1}$ and $5x10^{-4}$-$1x10^{-1}$ M), slopes of (53.98, 51.45, 49.66 and 48.98 mV/decade) and with detection limits ($5x10^{-5}$ M, $2x10^{-5}$ M, $3x10^{-5}$ M and 1×10^{-5}M) respectively. The results are summarized in Table 3-1. The electrode (A1), is the best electrode since it gives a Nernstian slope of 53.98 mV/decade and correlation coefficient 0.9999. The 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.[110]

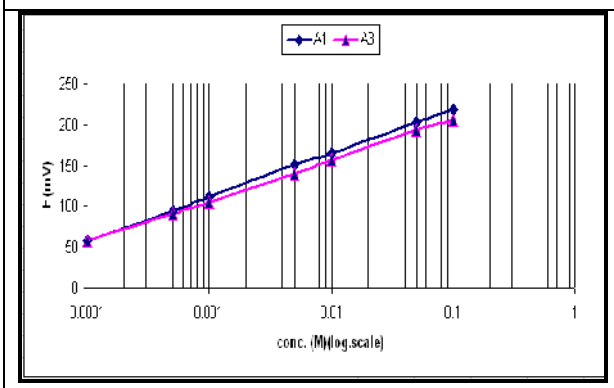
Electrode no.	Electrode membrane	Slope (mV/Decade)	Linear concentration range (M)	Detection limit (M)	Response time (sec)			Lifetime (day)
					10^{-2} (M)	10^{-3} (M)	10^{-4}(M)	
A1	**CPP+TPB+DBPH**	53.98	1×10^{-4}– 1×10^{-1}	5×10^{-5}	25	15	10	50
A2	**CPP+TPB+DBP**	51.45	5×10^{-4}–1 $\times10^{-1}$	2×10^{-5}	30	18	12	15
A3	**CPP+TPB+DOP**	49.66	1×10^{-4} –1× 10^{-1}	3×10^{-5}	35	20	14	23
A4	**CPP+TPB+TBP**	48.98	5×10^{-4}– 1×10^{-1}	1×10^{-5}	45	35	15	21

Table 3-1:- The parameters of four (CPSS) electrodes.

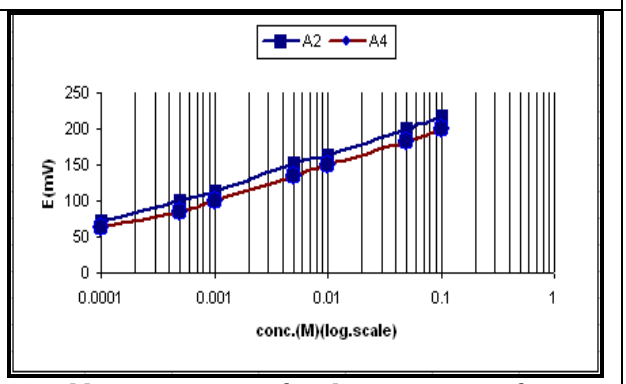
From the results obtained, electrode (A1) was considered to be more sensitive than the other electrodes because of its high slope value. The electrode (A4) gave non-Nernstian slope, this could be due to the low viscosity of TPB (3.114 cst) which causes a rapid leaching of the membrane components to the external solution. The electrode (A2), gave slope of 51.45 mV/decade due to the viscosity of the plasticizers; i.e. the high viscosity of the DBP (112.88 cst) plasticizer 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 unhomogenous between (DOP) and (PVC) and other components in the membrane.[110] The electrode parameters were obtained for electrode (A1) which gave a good response and stability in comparison with the other electrodes. The reproducibility of the potential response of the electrode (A1)[based on (DBPH)], was relatively good and the response properties of the proposed electrode did not changed obviously after using the electrode for about 50 days.



(a)Calibration curves of CPSS selective electrodes (A1, A2, A3 and A4).



(b)Calibration curves for linear range of CPSS electrodes (A1 and A3).



(c)Calibration curves for linear range of CPSS electrodes (A2 and A4).

Figure 3-1:- (a) Calibration curves of CPSS selective electrodes (A1, A2, A3 and A4), (b) Calibration curves for linear range of CPSS electrodes (A1 and A3), (c) Calibration curves for linear range of CPSS electrodes(A2 and A4).

The working range characteristics for (CPSS) sensors in the investigated electrodes were assessed on the basis of the calibration curves which were obtained by measuring of the potential values of the set of (CPSS) solutions ranged (10^{-1}-10^{-7}) as shown in Figure 3-1-(a) and as linear range for each electrode as shown in Figure3-1-(b) and (c). The parameters of four (CPSS) electrodes, equations of the linear range, slopes and correlation coefficients are listed in Table 3-2.

Table 3-2:- The equation of calibration curves, slopes and correlation coefficients for four (CPSS) electrodes.

Electrode no.	Electrode membrane	Linear equation	Slope (mV/decade)	Correlation coefficient (r)
A1	CPP+TPB+DBPH	y = 23.442 ln(x) + 273.5	53.98	0.9999
A2	CPP+TPB+DBP	y = 22.341 ln(x) + 267.81	51.45	0.9996
A3	CPP+TPB+DOP	y = 21.564 ln(x) + 255.47	49.66	0.9994
A4	CPP+TPB+TBP	y = 21.272 ln(x) +247.54	48.98	0.9998

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3-1-2- Effect of pH:-

The effect of pH on the electrode potentials for (CPSS) selective electrode (A1) was examined by measuring the potential 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). The pH was adjusted by adding appropriate amounts of hydrochloric acid and/or sodium hydroxide solution and the results as shown in Figure 3-2.

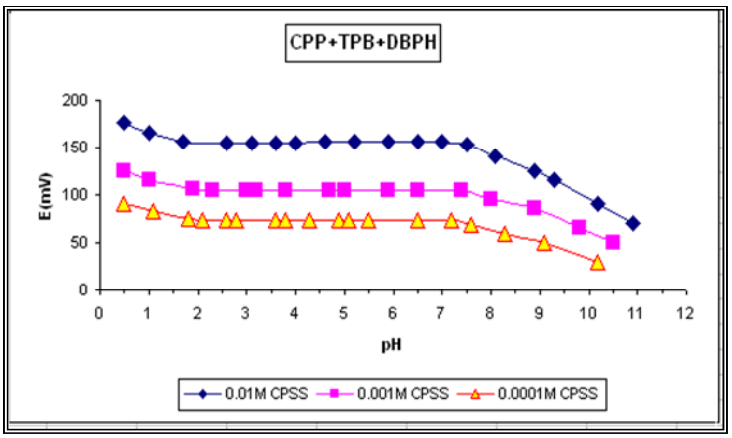


Figure 3-2- Effect of pH on the potential of the electrode A1 at concentrations 10^{-2}, 10^{-3} and 10^{-4} M.

At pH values less than 1.5 or in high acidity, the electrode response has been increased rather irregularly. This may be due to that the electrode starts to response to H^+ activities as well as analyte ions, and in an alkaline

solution (pH above 7) the electrode response starts to decrease, this may be attributed to the decreasing in the solubility of CPSS.[15] The working pH range are tabulated in Table 3-3.

Table 3-3:- Working pH ranges for CPSS electrode (A1).

Electrode 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

3-1-3-Selectivity methods:-

Potentiometric selectivity coefficient defines the ability of the ISE to differentiate a particular (primary) ion from others (interfering ions).[31]

3-1-3-1 Separate solution method:-

The potentials are measured with two separate solutions, one containing10 $^{-3}$M of CPSS, the other one containing 10^{-3}M from interfering species. The results obtained for selectivity coefficients calculated by using equation 1-4 are summarized in Table 3-4.

Table 3-4:- Selectivity coefficient values of electrode (A1), when E_{CPSS} =111.5 mV and the slope of 53.98 mV/decade.

Interfering species	E_B (mV) of 10^{-3} M	Log $K_{A,B}$	$K_{A,B}$
K^+	25	-1.602	2.49×10^{-2}
Na^+	32	-1.472	3.36×10^{-2}
Fe^{3+}	50	-3.149	7.09×10^{-4}
Al^{3+}	45	-3.241	5.73×10^{-4}
Cu^{2+}	40	-2.824	1.49×10^{-3}
Mn^{+2}	83	-2.027	9.37×10^{-3}
Sugrose	53	-1.083	8.24×10^{-2}
gelatine	45	-1.231	5.86×10^{-2}
Chloramphenicol palmitate	55	-1.046	8.91×10^{-2}

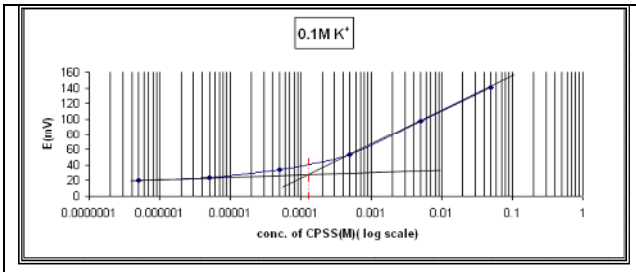
The interference effect of different organic and inorganic cations on the electrode response was evaluated, by measuring the selectivity coefficient $K_{A,B}$. The selectivity coefficient values for monovalent cations is higher than the values from di- and tri-valents cations, that may be due to differences in ionic size, charge, mobility and permeability, the order of the selectivity is:

monovalent > di-valent > tri-valent.[111]

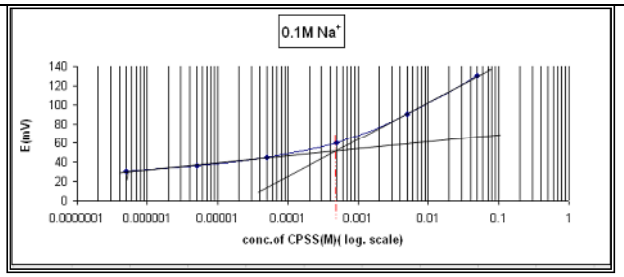
In most cases, no significant influence on the electrode performance was observed [all values of $K^{pot}_{A,B}$ were less than (0.1)]. This reflects a very high selectivity of the electrode A1 towards CPSS.

3-1-3-2- Mixed solution method:-

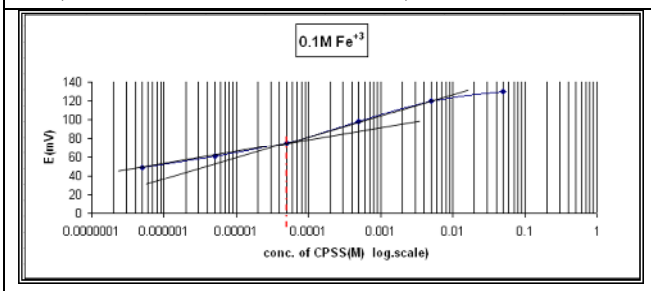
By using fixed interference method (FIM)[35,36], the potentials are measured at constant activity of the interfering ion (5×10^{-2}M of B) and varying activities of the primary ion (a_{CPSS}) . The potentials E (mV) values obtained are plotted vs. the logarithm of the activity of the primary ion. The intersection of the extrapolated linear portions of this plot indicates the value of (a_{CPSS}). Figure 3-3 (a, b, c, d, e, f, g, h, i) can be used to calculate $K^{pot}_{A,B}$ by using equation 1-5, all results of a_{CPSS} and $K^{pot}_{A,B}$ were in Table 3-5.



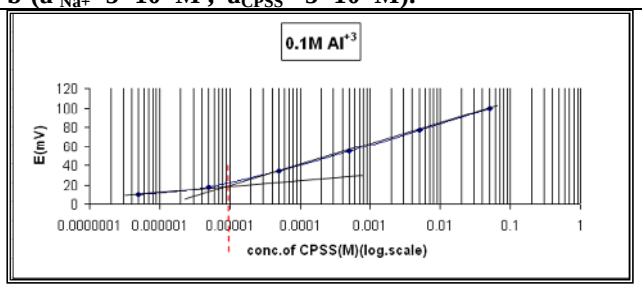
a- ($a_{K+}=5\times10^{-2}$M , $a_{CPSS}=1.4\times10^{-4}$).



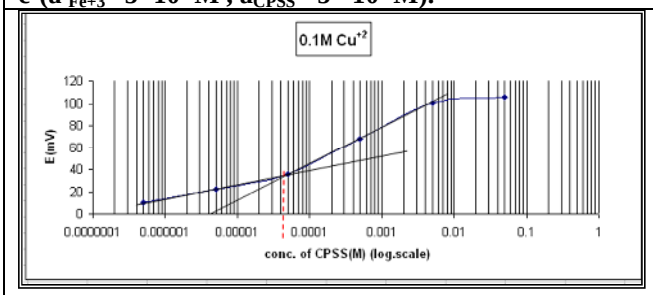
b-($a_{Na+}=5\times10^{-2}$M , $a_{CPSS}=5\times10^{-4}$M).



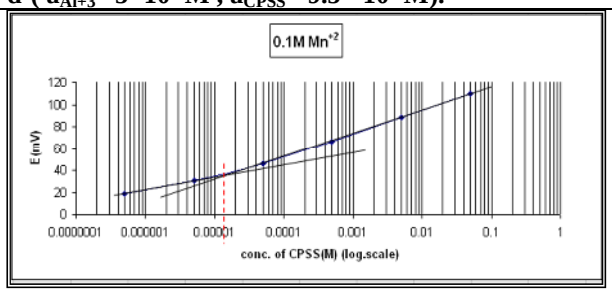
c-($a_{Fe+3}=5\times10^{-2}$M , $a_{CPSS}=5\times10^{-5}$M).



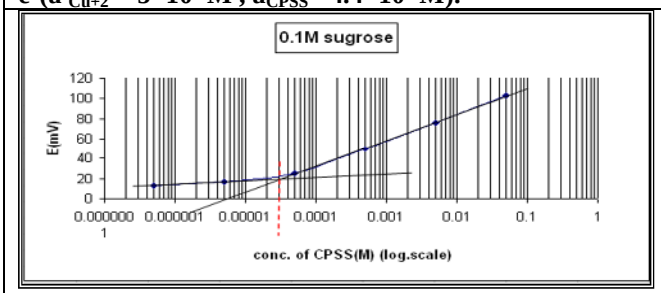
d-($a_{Al+3}=5\times10^{-2}$M , $a_{CPSS}=9.5\times10^{-6}$M).



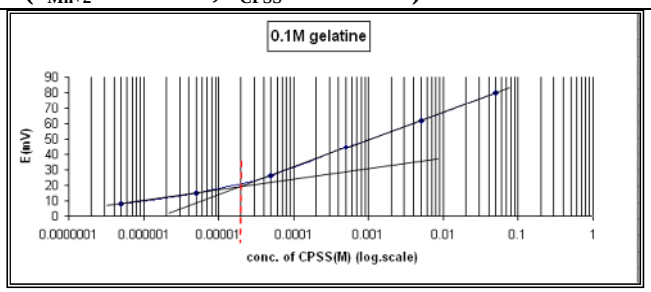
e-($a_{Cu+2}=5\times10^{-2}$M , $a_{CPSS}=4.4\times10^{-5}$M).



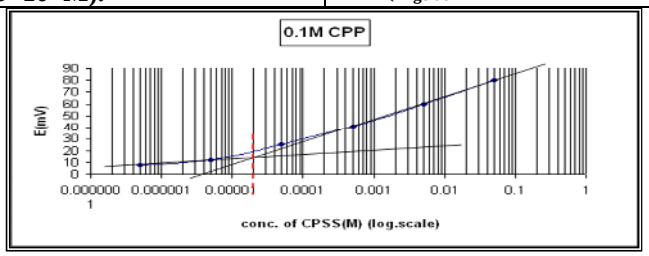
f-($a_{Mn+2}=5\times10^{-2}$M , $a_{CPSS}=1.5\times10^{-5}$M).



g-($a_{sucrose}=5\times10^{-2}$M , $a_{CPSS}=3\times10^{-5}$M).



h-($a_{gelatin}=5\times10^{-2}$M , $a_{A}=2\times10^{-5}$M).



i-($a_{CPP}=5\times10^{-2}$M , $a_{CPSS}=2\times10^{-5}$M).

Figure3-3:-FIM calibration curves (a, b, c, d, e, f, g, h, i) for electrode A1, when the activity of the interfering is constant.

Table 3-5:- Values of $K^{pot}_{A,B}$ according to FIM .

Interfering species	$a_B=5\times10^{-2}$	
	a_{CPSS}	$K^{pot}_{A,B}$
K^+	1.4×10^{-4}	2.80×10^{-3}
Na^+	5.0×10^{-4}	1.00×10^{-2}
Fe^{3+}	5.0×10^{-5}	1.34×10^{-4}
Al^{3+}	9.5×10^{-6}	2.55×10^{-5}
Cu^{2+}	4.4×10^{-5}	1.96×10^{-4}
Mn^{2+}	1.5×10^{-5}	6.70×10^{-5}
Sugrose	3.0×10^{-5}	6.00×10^{-4}
Gelatine	2.0×10^{-5}	4.00×10^{-4}
Chloramphenicol palmitate	2.0×10^{-5}	4.00×10^{-4}

In mixed solution method, the potentiometric selectivity coefficients were used to evaluate the degree of interference. additionally ,we can see the drift in the calibration curve when interfering ion reacts with analyte (CPSS) such as ($Cu^{2+}$and Fe^{3+}) as shown in Figure 3-3-(c) and (e).

3-1-4- Sample analyses:-

Four different potentiometric techniques were used for the determination of (CPSS) including, Direct method, Standard addition method (SAM), Multiple standard additions method (MSA) and potentiometric Titration by using electrode (A1). The recovery (Re %), relative error (E_r %) and relative standard deviation (RSD %) for each method are calculated.

3-1-4-1- Direct method:-

This is the simplest method of obtaining quantitative results using ISEs. The calibration curve was constructed (for electrode A1) and the concentration of the unknown was calculated from the linear equation that obtained from calibration curve (y = 23.442 Ln(x) + 273.5). The results of calculation for five replicate reading for 10^{-4}M CPSS are listed in Table 3-6.

Table 3-6:- The results of five samples of (CPSS) standard solution 10^{-4} M using direct method for electrode (A1), where slope=53.98 mV/decade.

Potential reading E(mV)	conc. of (CPSS) sample calculated from linear equation/(M)	S*	$\overline{X} \pm (ts/\sqrt{N})$	Re%	E_r%	RSD%
57.50	0.996×10^{-4}	4.764×10^{-7}	$0.996 \times 10^{-4} \pm 0.592 \times 10^{-6}$	99.6%	-0.4%	0.477%
57.56	0.998×10^{-4}			99.8%	-0.2%	
57.49	0.995×10^{-4}			99.5%	-0.5%	
57.40	0.991×10^{-4}			99.1%	-0.9%	
57.70	1.004×10^{-4}			100.4 %	0.4%	

S*: standard deviation, t=2.78, N= 5.

3-1-4-2- Incremental Methods:-

3-1-4-2-1- Standard additions method (SAM):-

The procedure for this method is that 0.5 ml increments of 10^{-2}M (CPSS) as standard was added to 20 ml of 10^{-3}M CPSS sample as unknown. The conc. of CPSS as unknown was found depending on the measurement potential using the proposed electrode (A1) and equation 1-8, Recovery, Relative error and Relative standard deviation for five additions of (CPSS) are listed in Table 3-7.

Table3-7:-Calculation for five additions of (CPSS) standard solution using (SAM) for electrode (A1) where slope=53.98, at concentration of sample 10^{-3} M.

V_S (mL) added	E/(mV)	ΔE	(V_U/V_S)	Antilog (ΔE/S)	C_U/(M)	S*	$\overline{X} \pm (ts/\sqrt{N})$	Re%	E_r %	RSD%
0.0	111.8	--------	--------	--------	----------	7.563×10^{-6}	$1.001 \times 10^{3} \pm 0.940 \times 10^{-5}$	----------	----------	0.754%
0.5	116.4	4.6	40.0	1.2167	1.010×10^{-3}			101.0%	1%	
1.0	120.1	8.3	20.0	1.4248	1.007×10^{-3}			100.7%	0.7%	
1.5	123.2	11.4	13.3	1.6262	1.004×10^{-3}			100.4%	0.4%	
2.0	125.9	14.1	10.0	1.8247	0.992×10^{-3}			99.2%	-0.8%	
2.5	128.1	16.3	8.0	2.0043	0.996×10^{-3}			99.6%	-0.4%	

***S*: standard deviation*, t=2.78, N= 5.**

3-1-4-2-2- Multiple standard additions method (MSA):-

The calibration curve for MSA for electrode (A1) was shown in Figure 3-4 by plotting antilog (E/S) versus the volume of the five different additions of 10^{-2} M of standard (CPSS) to 20 ml of 10^{-3}M of unknown. From the equation of the calibration curve the volume (mL) at intercept with X axis for the curve was calculate which equal to 2.515, then the concentration be calculated by using equation 1-11. The volume at intercept with X axis, concentration of the unknown sample (C_U), the analysis results %Re and %E_r are listed in Table 3-8.

Vol. (mL) of std. add	E / mV	Antilog(E/S)
0.0	111.8	117.7979
0.5	116.4	143.3356
1.0	120.1	167.841
1.5	123.2	191.5697
2.0	125.9	214.9539
2.5	128.1	236.1028

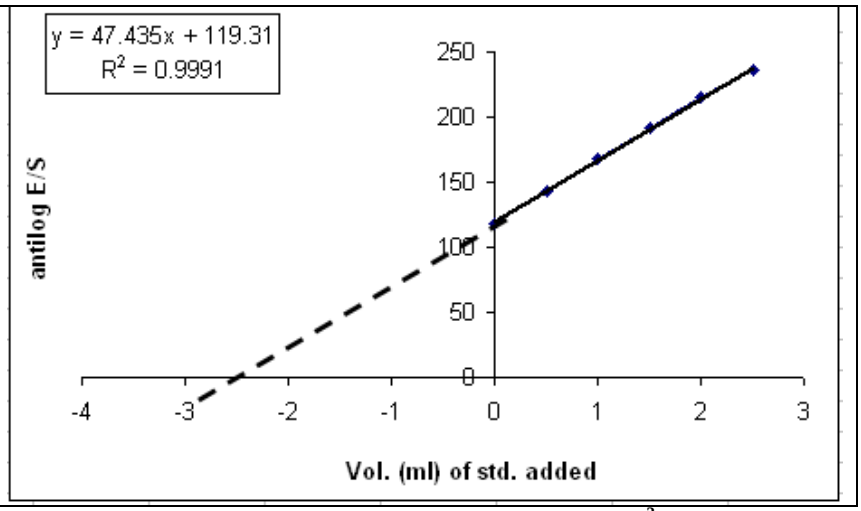


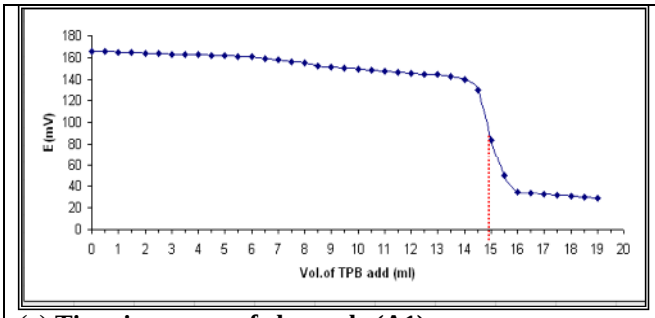
Figure3-4:- Calibration curve of antilog (E/S) versus the volume added of standard (10^{-2} M) for determination of 20mL (CPSS) solution 10^{-3} M by (MSA).

Table 3-8:- The linear equation of calibration curve uses MSA, correlation coefficient, volume at intercept, the concentration of sample (C_U), Re% and E_r% for the unknown sample.

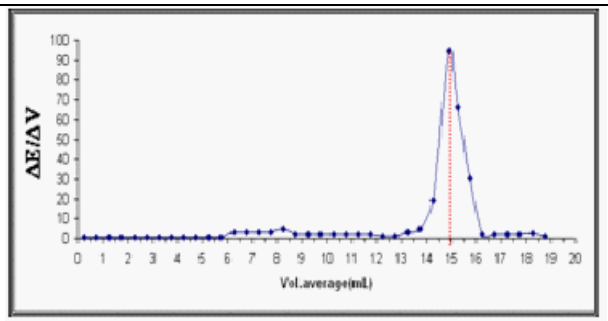
Linear equation	r	Volume at intercept (mL)	CU(M)	Re%	E_r%
Y=47.401x+119.24	0.9995	2.515	1.006×10^{-3}	100.6%	0.6%

3-1-4-2-3-Titration method:-

The potentiometric titration for 15 mL of 0.01M CPSS sample solution with 0.01M TPB as titrant solution as shown in Figure 3-5-(a) and (b). The results of titration (Re%, E_r% and RSD%) are listed in Table 3-9.



(a) **Titration curve of electrode (A1).**



(b) **Titration curve of electrode (A1) by using first derivative.**

Figure 3-5:- (a) Titration curve of electrode (A1) for 15 mL sample solution 0.01 M CPSS with 0.01 M of TPB as a titrant solution,(b) Titration curve of electrode (A1) by using first derivative, 15 mL sample solution 0.01 M CPSS with 0.01 M of TPB as a titrant solution.

Table 3-9:-The results of using titration method for standard CPSS sample for electrode (A1).

Titration Figure	Vol. mL at the end point	C_U(M)	Re%	E_r%	RSD*%
Figure 3-5-(a)	14.8	0.986×10^{-2}	98.6 %	-1.4 %	0.500%
Figure 3-5-(b)	14.9	0.993×10^{-2}	99.3%	-0.7%	

RSD* % for the unknown concentration from the two figures.

3-1-5-Analyses pharmaceutical preparations via electrode (A1):-

Electrode (A1) was proved to be useful in the potentiometric determination of chloramphenicol sodium succinate, Therefore it was used for the determination of the drug in pharmaceutical preparations and the data obtained for pharmaceutical samples were listed in Table 3-10.

Table 3-10:- sample analyses of chloramphenicol sodium succinate injection pharmaceutical using electrode (A1).

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}
Weight(g)	0.4464	0.4464	0.4464	0.4464
Found(M)	0.998×10^{-3}	1.001×10^{-3}	1.004×10^{-3}	0.999×10^{-3}
gm / vial	0.9999	0.9998	0.9999	0.9998
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}	----------	----------
$\bar{x}\pm$ (ts/√N)	$0.998\times10^{-3}\pm0.829\times10^{-5}$	$1.001\times10^{-3}\pm0.112\times10^{-4}$	----------	----------

RSD*% for n=5, t=2.78

3-1-6-Derivative Spectrophotometry (DS):-

3-1-6-1-First Derivative (^{1}D):

First-derivative (^{1}D) spectra for CPSS solutions 2-64 mg/L have been taken from normal using scale factor=10. Figure 3-6, shows first-derivative spectra of CPSS. ^{1}D spectrum of CPSS show a peak (P) at 258 nm and a valley (V) at 300 nm. But all peaks and valleys below 220 nm gave a noisy signal, which contained the absorption of impurities.

The calibration curves were constructed for these two wavelengths (258 nm and 300 nm) as shown in Figures 3-7 and 3-8.

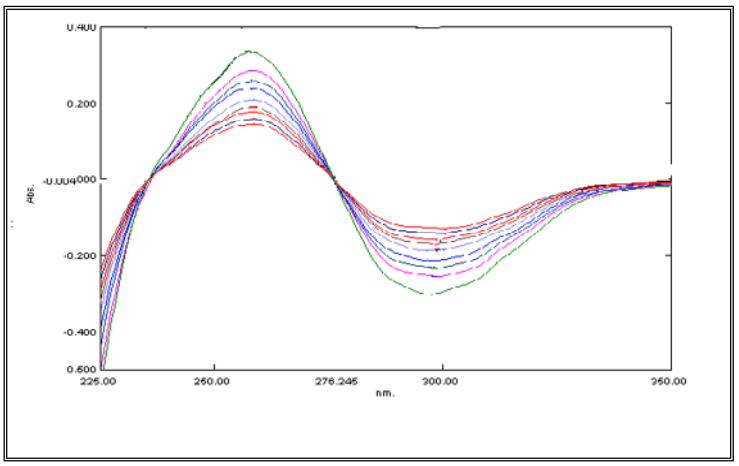


Figure 3-6:- The first derivative spectra for CPSS solutions 2-64 mg/L.

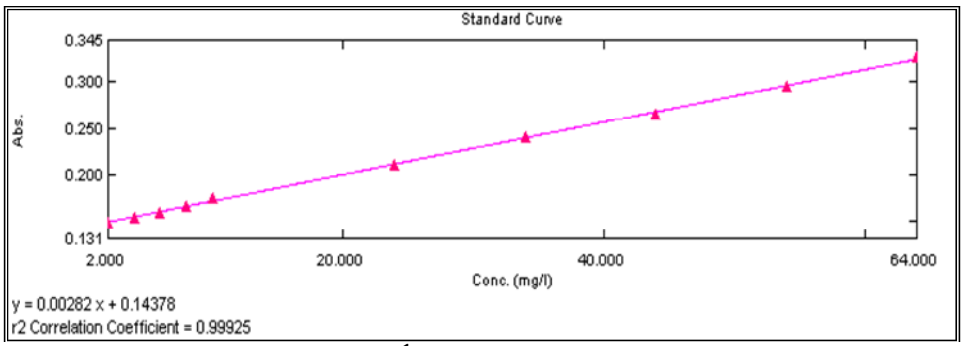


Figure 3-7:- Calibration curve of ^{1}D spectrum for CPSS at λ 258 nm at different concentration range from 2 to 64 mg/L.

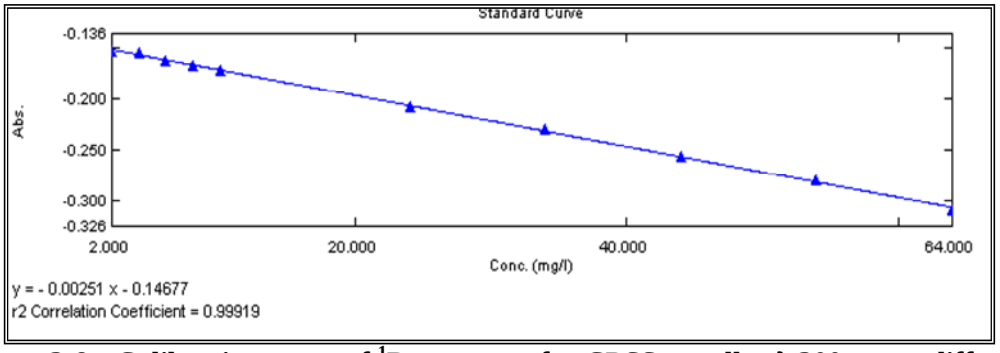


Figure 3-8:- Calibration curve of ^{1}D spectrum for CPSS at valley λ 300 nm at different concentration range from 2 to 64 mg/L.

Figure 3-7 shows the calibration curve of first-derivative at the λ 258 nm, from the linear equation of the calibration curve (Y = 0.00282X +0.14378) the concentration of the unknown samples can be calculated . The results of 10^{-4}M CPSS are listed in Table 3-11.

Table 3-11:-Calculation for five samples of CPSS standard solution 10^{-4}M (44.04 mg/L) by using direct method for calibration curve of ^{1}D spectra of UV-spectrophotometry at λ (258nm).

Abs.	C_U (mg/L)	C_U (M)	S*	$\overline{X} \pm (ts/\sqrt{N})$	Re%	E_r%	RSD* %
0.268	44.04	0.991×10^{-4}	6.942×10^{-7}	$1.001\times10^{-4}\pm0.863\times10^{-6}$	99.1%	-0.9%	0.693%
0.271	44.52	1.005×10^{-4}			100.5%	0.5%	
0.269	44.41	0.997×10^{-4}			99.7%	-0.3%	
0.270	44.73	1.007×10^{-4}			100.7%	0.7%	
0.267	44.60	1.006×10^{-4}			100.6%	0.6%	

S*: standard deviation; t=2.78; N=5.

The calculated linear equations for first-derivative, correlation coefficients and the range of concentrations for each calibration curve are listed in Table 3-12.

Table3-12:- Calculation linear equations, correlation coefficient and the range of concentrations for the first derivative.

Method	λ (nm)	Conc. Rang mg.ml^{-1}	Linear equation	r^2
^{1}D	P=258	2-64	Y=0.00282X+0.14378	0.99925
	V=300	2-64	Y=0.00251X+0.14677	0.99919

3-1-7-Comparison between ISE and first derivative methods:

The results of comparison between first derivative (^{1}D) and direct method of ion selective electrode by using F-test are shown in the Table 3-13. The analytical methods results were showed to be simple, rapid and with a good precision by comparing between first derivative (^{1}D) and direct method of ion selective electrode by using F-test at 95% confidence limit.

Table 3-13:- 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
0.996×10^{-4}	4.764×10^{-7}	0.991×10^{-4}	6.942×10^{-7}	2.1233
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 $S_1 > S_2$, $F_{table}=6.39$.

Since $F_{calculate} < F_{table}$, we conclude that there is no significant difference precision between the two methods.

3-2- Iron (III) electrodes:-

3-2-1-The FTIR spectra for chloramphenicol sodium succinate and chloramphenicol sodium succinate-iron (III):-

The CPSS and complex [CPSS-Fe(III)] are characterized by their FTIR spectra as shown in Figure 3-9 and Figure 3-10 for CPSS alone and for [CPSS-Fe(III)] complex respectively. The absorption bands of functional groups for both CPSS and the complex are listed in Table 3-14.

Table 3-14:- The functional groups obtained from the spectrum for CPSS and complex [CPSS-Fe(III)].

Functional group	CPSS cm^{-1}	Complex [CPSS-Fe(III)] cm^{-1}
ν (O-H) +(N-H)	3400	3361.7
ν (C-H) aliphatic	2864	2927.7
ν (C-H) aromatic	2299	2376.1
ν (C=O) ester	1749	1740
ν (C=C)	1350.1	1598.9
ν (C-O) ester	1164.9	1118.6
ν (ˉO-N=O)	1250 1519.8	1350.1 1521.7
(C=O) amide	1691.5	1685.7
δ para sub.benzene	813.9	812.0
δ (C-Cl)	665.4	609.5
δ (C-N)	860.2	812.0
ν (Fe-N)	-	422.4
δ (N-H) bending amide	1573.8	1598.9

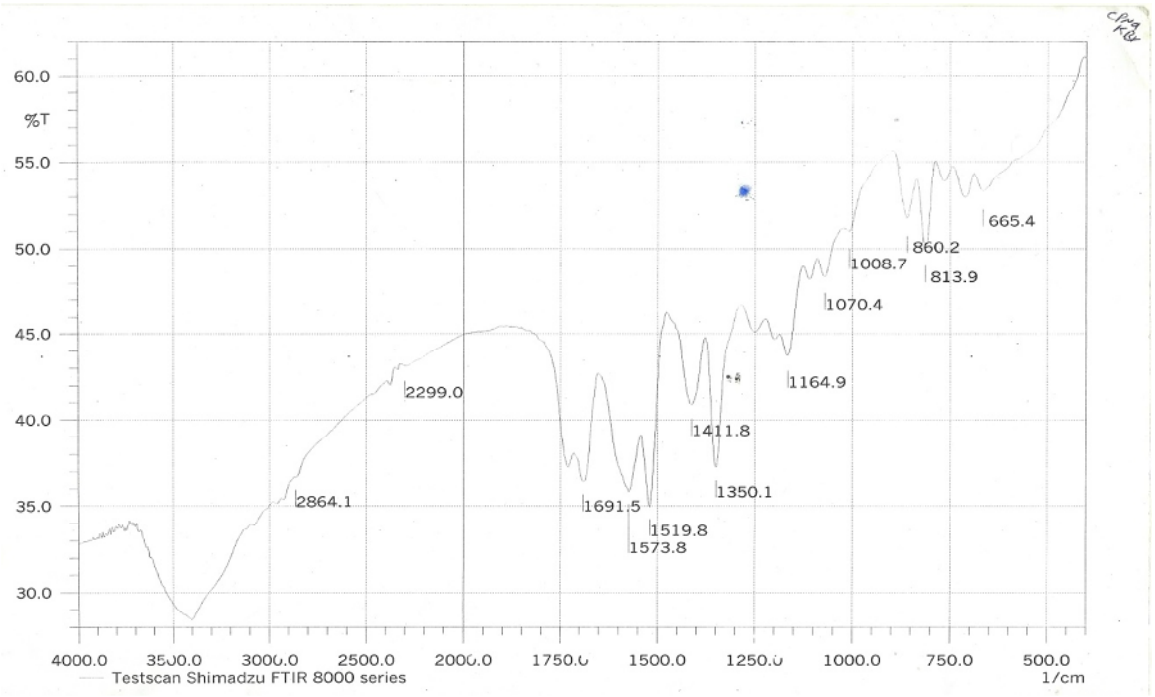


Figure 3-9:- FTIR spectra for CPSS by using KBr.

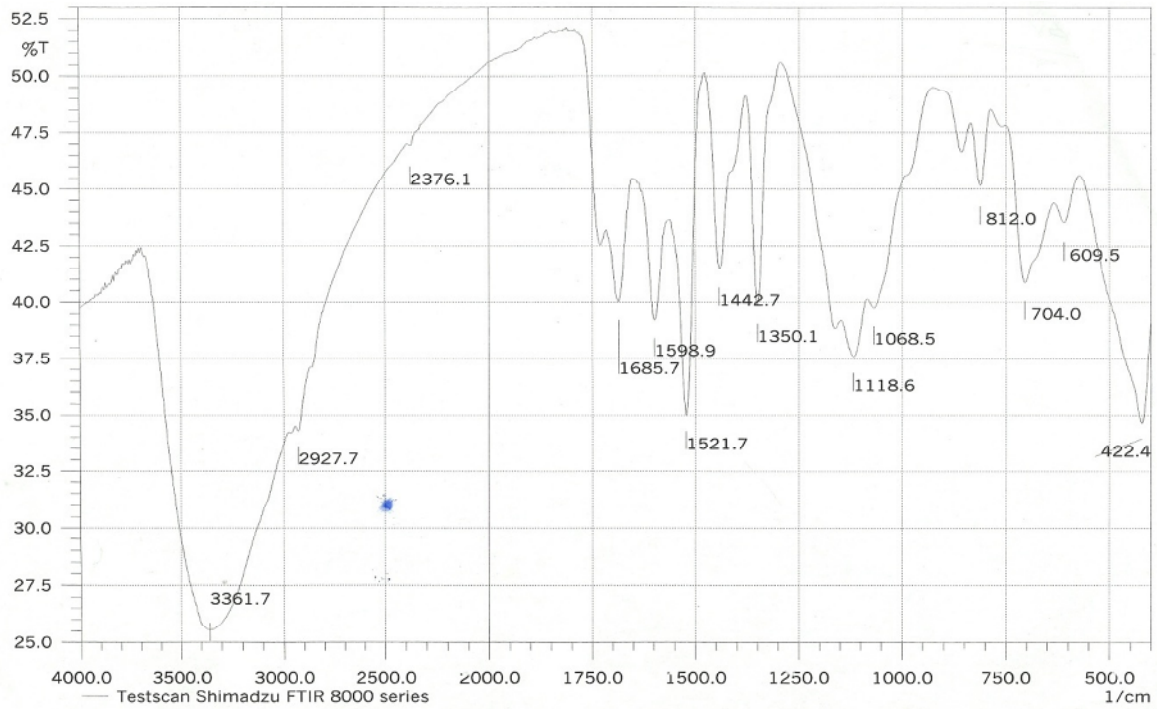
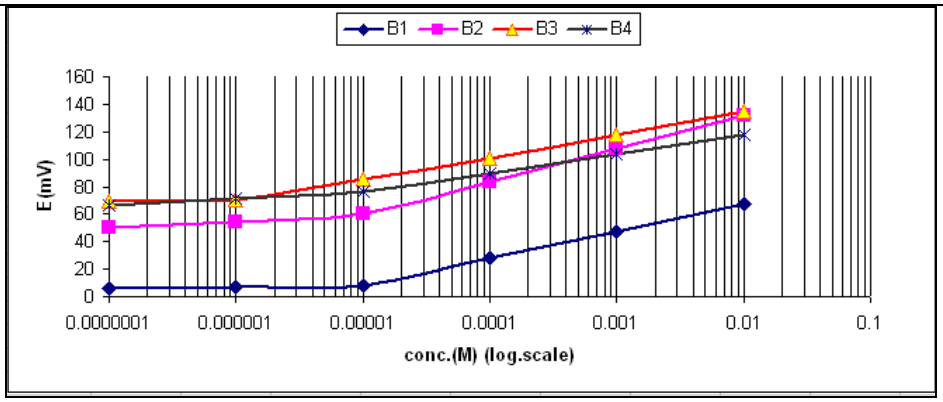


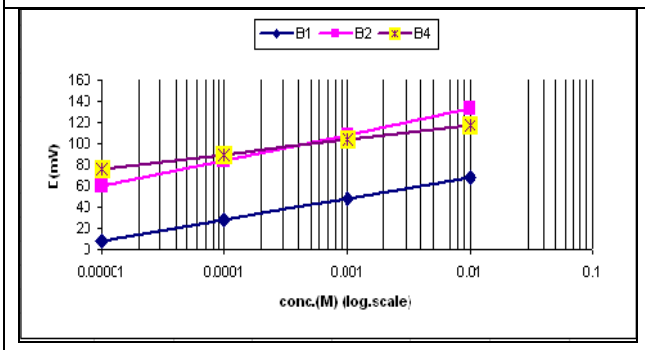
Figure 3-10:- FTIR spectra for [CPSS-Fe(III)]complex by using KBr.

3-2-2-Iron(III) sensor characteristics:-

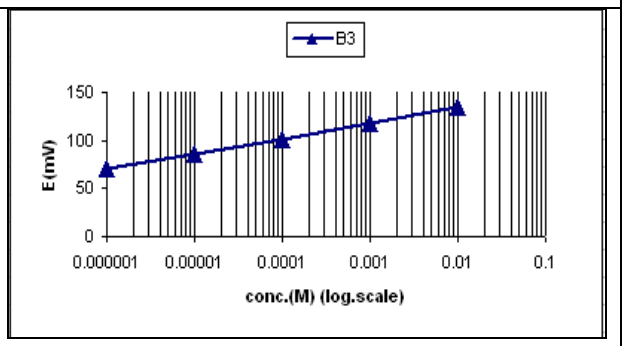
New four iron(III) selective electrodes (B1, B2, B3, B4) based on using [CPSS-Fe(III)] ion-pair complex as the electro-active material and four plasticizers; Di-butyl phosphate (DBP); Di-butyl phthalate (DBPH); Di-octyl phthalate (DOP): Tri-butyl phosphate (TBP); in PVC matrix were examined respectively. The effects of different plasticizers were studied with respect to the linear concentration range, slope, detection limit, response time and lifetime. The electrode with good characteristics was used for further studies. The calibration curves for iron (III) selective electrodes (B1, B2, B3 and B4) are show in Figure 3-11-(a), (b) and (c), the electrodes gave linear ranges from ($1x10^{-5}$-$1x10^{-2}$ M, $1x10^{-5}$-$1x10^{-2}$ M, $1x10^{-6}$-$1x10^{-2}$ M and $1x10^{-5}$-$1x10^{-2}$ M), slopes of (19.79, 24.60, 16.01 and 13.82 mV/decade),with detection limit ($9x10^{-6}$ M, $7x10^{-5}$ M, $2x10^{-6}$ M and 9×10^{-5}M) respectively. B1 electrode is the best electrode that gave the Nernstian slope of 19.79 mV/decade, with liner range $1x10^{-2}$–$1x10^{-5}$ M. This may be due to the compatibility between the components of the membrane, and the viscosity of DBP effect on the ion exchange between the membrane ions and the external solution ions. Consequently, DBP is more effective solvent mediator than other plasticizer due to its large dielectric constant. The long lifetime and good stability and reproducibility of electrode (B1) may be due to a high viscosity (≈112.88 CST), which prevents the leaching of complex to the external solution and causes a low mobility of ions in the matrix of the membrane.



(a)Calibration curves of iron(III) selective electrodes (B1, B2, B3 and B4).



(b)Calibration curves for linear range of iron(III) electrodes (B1, B2 and B4).



(c)Calibration curve for linear range of iron(III) electrode (B3).

Figure 3-11:- (a) Calibration curves of iron(III) selective electrodes (B1, B2, B3 and B4), (b) Calibration curves for linear range of iron(III) electrodes (B1, B2 and B4), (c) Calibration curve for linear range of iron(III) electrode (B3).

B2 electrode, gave a slope of 24.60 mV/decade. This high slope may be due the viscosity of DBPH which make steric in the ion exchange between ion-pair of complex [CPSS-Fe(III)] in membrane and the external solution. But the B4 electrode gave non-nernst slope of 13.82mV/decade. This may be attributed to the low viscosity of TBP (3.11) and lead to leaching of the complex from the membrane to the external solution as well as decrease ion-exchange process between ion-pair of complex [CPSS-Fe(III)] in membrane and the external solution of, or may be attributed to the steric factor . The liner equation, slope, correlation coefficient and the results are listed in Table 3-15.

Table 3-15:-The equation of calibration curves, slope and correlation coefficient for four iron (III) electrodes.

Electrode no.	Electrode membrane	Linear equation	Slope mV/Decade	Correlation coefficient (r)
B1	**CPSS-Fe(III)+DBP**	y = 8.5947ln(x) + 107.29	19.79	0.9999
B2	**CPSS-Fe(III)+DBPH**	y = 10.6840 ln(x) + 182.60	26.60	0.9997
B3	**CPSS-Fe(III) +DOP**	y = 6.9531 ln(x) + 165.74	16.01	0.9994
B4	**CPSS-Fe(III)+TBP**	y = 6.0019 ln(x) + 145.27	13.82	0.9998

The response time for each of the four electrodes (B1, B2, B3 and B4) to reach a stable potential within ±1 mV of the final equilibrium value was determined. The dynamic response time was recorded at different concentrations of iron (III) solution. It was observed that during the long time period of 37 days. Then after 37 days, the electrode (B1) characteristics significantly drifted away from the Nernst behavior. This may be attributed to the decrease in the quantity of ionophore which means that the complex and the plasticizer in the membrane are migrated from the PVC membrane into the PVC tube. Table 3-16 shows the response times, detection limits, liner ranges and life times for these electrodes.

Table 3-16:- The linear range, detection limit, response time and lifetime for iron (III) electrodes.

Electrode no.	Electrodes membrane	Linear range (M)	Detection limit (M)	Response time (sec)			Life time (day)
				10^{-2}(M)	10^{-3}(M)	10^{-4} (M)	
B1	**CPSS- Fe (III) +DBP**	1×10^{-2}– 1×10^{-5}	9×10^{-6}	20	10	5	37
B2	**CPSS- Fe(III) +DBPH**	1×10^{-2}– 1×10^{-5}	7×10^{-5}	40	35	25	41
B3	**CPSS- Fe(III)+DOP**	1×10^{-2}– 1×10^{-6}	2×10^{-6}	25	15	10	23
B4	**CPSS- Fe(III) +TBP**	1×10^{-2}– 1×10^{-5}	9×10^{-5}	45	30	15	16

3-2-3- Effect of pH on electrode B1 potential:-

The values of the measured potential for [CPSS-Fe(III)+DBP] electrode (B1) remains nearly constant at 1.5-6 pH range as shown in Figure 3-12. This represented that the proposed electrode can be used to measure iron (III) solutions without pH adjustment. At pH lower than 1.5, the hydrogen ions diffuse through the membrane until an equilibrium is reached between the external and internal concentrations. But at pH higher than 6, some iron (III) hydroxide was form in the solution [96], this causes deviation in the electrode response. The results prove that electrode potentials are affected by pH values. The working pH were tabulated in Table 3-17.

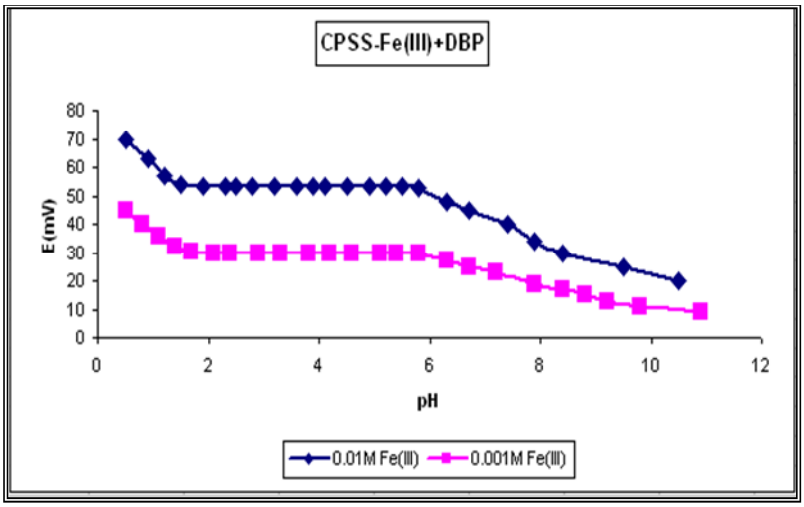


Figure 3-12:- Effect of pH on the potential of the electrode B1, at concentrations 10^{-2} and 10^{-3} M.

Table 3-17:- Working pH ranges for electrode B1.

Electrode no.	Composition of electrode B1	pH range	
B1	(CPSS-Fe(III) +DBP)	[Fe(III)]10^{-2}M	[Fe(III)]10^{-3}M
		1.5-6	2-6

3-2-4-Selectivity methods for electrode B1:-

3-2-4-1-Separate solution methods:-

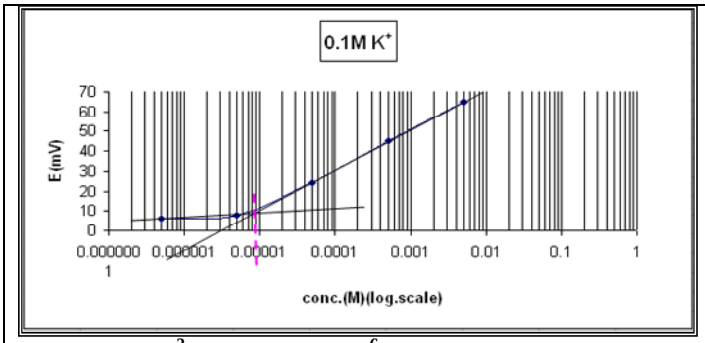
In this method, the potentials are measured for two separate solutions in same concentration ($a_{Fe(III)}=a_B=10^{-3}$M), the value of $K^{pot}_{A,B}$ is calculated by the equation 1-4. The results of selectivity coefficients are summarized in Table 3-18.

Table3-18:- Selectivity coefficient values for electrode B1, when $E_{Fe(III)}$=47.7mV and the of slope 19.79mV/decade.

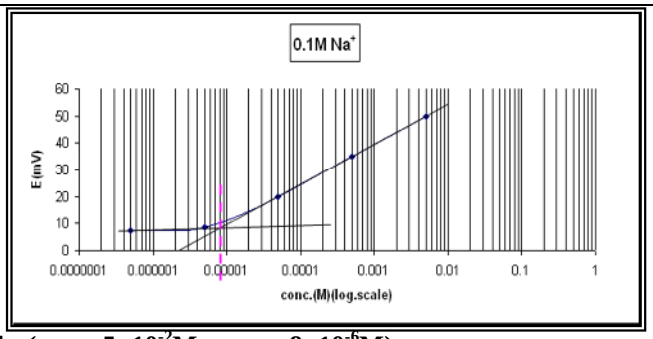
Interfering species	E_B (mV)	Log $K^{pot}_{A,B}$	$K^{pot}_{A,B}$
K^+	-120	-2.473	3.35×10^{-3}
Na^+	-130	-2.979	1.04×10^{-3}
Cu^{2+}	-35	-2.678	2.09×10^{-3}
Mn^{2+}	-20	-1.920	1.19×10^{-2}
Zn^{2+}	-30	-2.426	3.74×10^{-3}
Al^{3+}	40	-0.389	4.08×10^{-1}
Folic acid	-125	-2.726	1.87×10^{-3}

3-2-4-2-Mixed solution methods:-

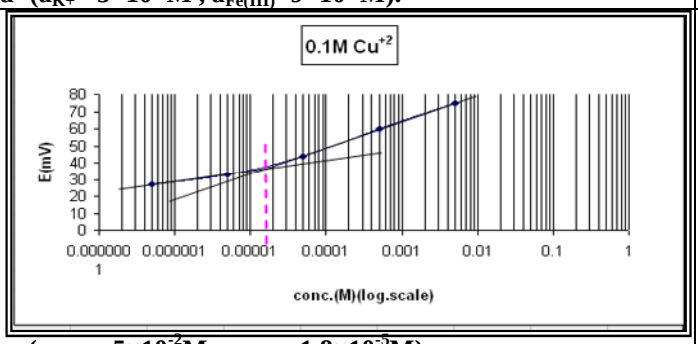
In this method, the potentials are measured for solutions of constant activity of the interfering ion (a_B) 5×10^{-2}M with varying activities of the primary ion that is for iron (III) ion ($a_{Fe(III)}$). Figure 3-13-(a, b, c, d, e, f, g) can be used to calculate $K^{pot}_{A,B}$ according to equation 1-5. All results of $K^{pot}_{A,B}$ were in Table 3-19.



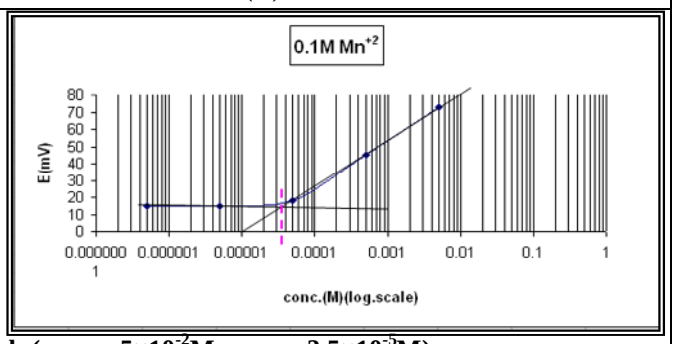
a- (a_{K+}= 5×10^{-2}M , $a_{Fe(III)}$=9×10^{-6}M).



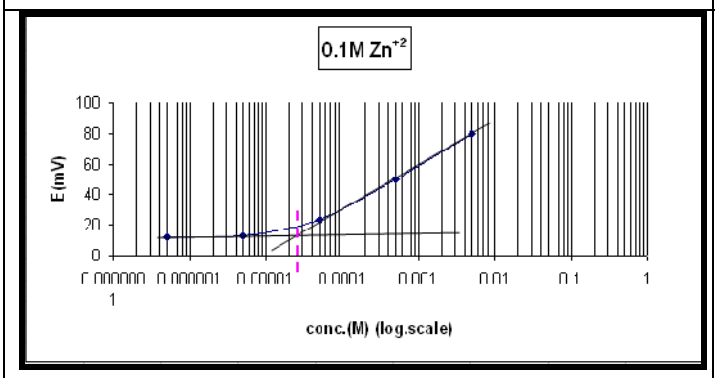
b- (a_{Na+}=5×10^{-2}M, $a_{Fe(III)}$=8×10^{-6}M).



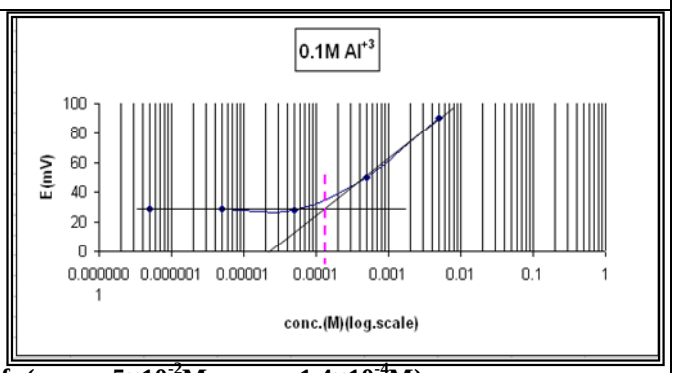
c- (a_{Cu+2}=5×10^{-2}M, $a_{Fe(III)}$=1.8×10^{-5}M).



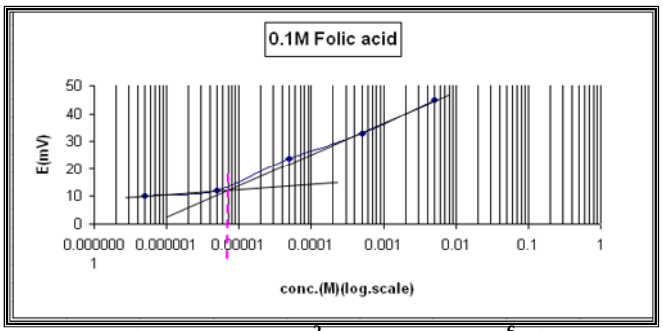
d- (a_{Mn+2}=5×10^{-2}M, $a_{Fe(III)}$=3.5×10^{-5}M).



e-(a_{Zn+2}=5×10^{-2}M, $a_{Fe(III)}$=2.5×10^{-5}M).



f- (a_{Al+3} =5×10^{-2}M, $a_{Fe(III)}$=1.4×10^{-4}M).



g- ($a_{Folic\ acid}$ =5×10^{-2}M, $a_{Fe(III)}$=7×10^{-6}M).

Figure3-13:-FIM calibration curves from (a, b, c, d, e, f, g) for electrode B1, when the activity of the interfering is constant.

Table 3-19:- Values of $K^{pot}_{A,B}$ according to FIM.

Interfering species	$a_B = 5\times10^{-2}$ M	
	$a_{Fe(III)}$	$K^{pot}_{A,B}$
K^+	9.0×10^{-6}	7.2×10^{-2}
Na^+	8.0×10^{-6}	6.4×10^{-2}
Cu^{2+}	1.8×10^{-5}	1.6×10^{-3}
Mn^{2+}	3.5×10^{-5}	3.1×10^{-3}
Zn^{2+}	2.5×10^{-5}	2.2×10^{-3}
Al^{3+}	1.4×10^{-4}	2.8×10^{-3}
Folic acid	7.0×10^{-6}	5.6×10^{-2}

3-2-5- Analyses of iron (III):-

3-2-5-1- Direct method for electrode B1:-

A calibration curve was constructed (for electrode B1) and the concentration of unknowns were calculated from the linear equation in Table 3-15.The results of calculation for five reading for 10^{-4} M iron(III) are listed in Table 3-20.

Table 3-20:- Calculation for five samples of iron (III) standard solution 10^{-4} M using direct method for electrode (B1) where slope=19.79.

Potential reading E(mV)	The conc. of iron(III) solution calculated from linear equation/(M)	S*	$\overline{X} \pm (ts/\sqrt{N})$	Re %	E_r%	RSD%
28.11	0.997×10^{-4}	5.029×10^{-7}	$1.0024\times10^{-4}\pm0.625\times10^{-6}$	99.7%	-0.3%	0.501%
28.15	1.002×10^{-4}			100.2%	0.2%	
28.12	0.998×10^{-4}			99.8%	-0.2%	
28.20	1.008×10^{-4}			100.8%	0.8%	
28.19	1.007×10^{-4}			100.7 %	0.7%	

S*: standard deviation, t=2.78; N= 5.

3-2-5-2- Incremental methods for electrode B1:-

3-2-5-2-1 -Standard additions method (SAM):-

It was carried out by a procedure that 0.5 mL increment of 10^{-2}M iron (III) as standard was added to 20 mL of 10^{-3}M iron(III) sample as unknown. The concentration of unknown is calculated by using equation 1-8. The results of calculated concentrations of unknown by using electrode B1, recoveries, relative errors and relative standard deviations for five additions of iron (III) are listed in Table 3-21.

Table 3-21:- Calculation for five additions iron (III) standard solution using (SAM) for electrode B1, where slope=19.79mV/decade, for 10^{-3} M sample.

V_S (mL) added	E (mV)	ΔE	(V_U/V_S)	Antilog (ΔE/S)	C_U/(M)	S*	X±(ts/√N)	Re%	E_r%	RSD%
0.0	47.40	--------	-------	--------	----------	4.266×10^{-6}	$0.9992\times10^{-3}\pm0.530\times10^{-5}$	----------	----------	0.426%
0.5	49.41	1.71	40.0	1.2201	0.997×10^{-3}			99.7%	-0.3%	
1.0	50.76	3.06	20.0	1.4276	1.001×10^{-3}			100.1%	0.1%	
1.5	51.92	4.22	13.3	1.6339	0.993×10^{-3}			99.3%	-0.7%	
2.0	52.82	5.12	10.0	1.8143	1.004×10^{-3}			100.4%	0.4%	
2.5	53.65	5.95	8.0	1.9982	1.001×10^{-3}			100.1%	0.1%	

S*: standard deviation, t=2.78; N=5.

3-2-5-2-2- Multiple standard additions method (MSA):-

The calibration curve for MSA obtained with electrode (B1) is shown in Figure 3-14 by plotting antilog (E/S) versus the added volumes of the five additions of standard iron (III) solution. The value of volume obtained at intercept with X axis, the concentration of the unknown sample (C_U) and the analysis results are listed in Table 3-22.

Vol.(mL) of std. add	E(mV)	Antilog (E/S)
0.0	47.70	257.2
0.5	49.41	313.8
1.0	50.76	367.2
1.5	51.92	420.2
2.0	52.82	466.6
2.5	53.65	514.0

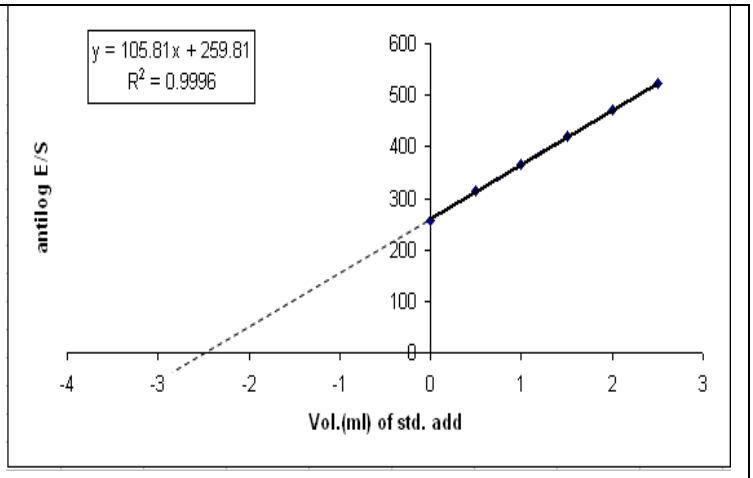


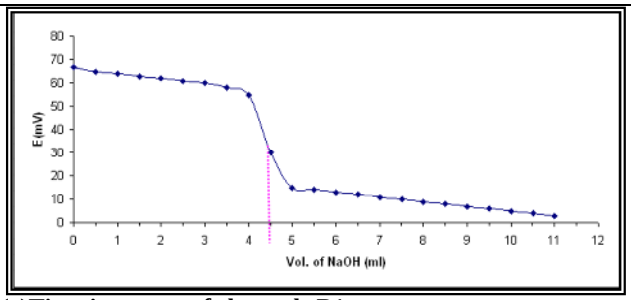
Figure 3-14:- Calibration curve of antilog (E/S) versus the volume added of standard 10^{-2}M for determination of 20 mL iron (III) solution 10^{-3}M by (MSA).

Table 3-22:- The linear equation of the calibration curve, correlation coefficient, volume at intercept, the concentration of sample (C_U), E_r% and Re% of the unknown sample.

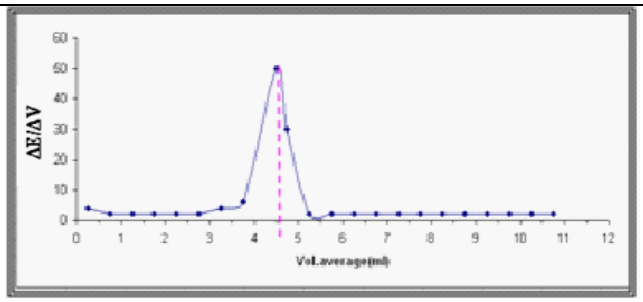
Linear equation	r	Volume at intercept (mL)	C_U(M)	Re%	E_r%
Y=105.81x+259.81	0.9997	2.455	0.982×10^{-3}	98.2%	-1.8%

3-2-5-2-3 -Titration method :-

A potentiometric titration for 15 mL of 0.01M of iron(III) solution with 0.1 M of sodium hydroxide (NaOH) as titrant solution was carried out . Figure 3-15-(a) and (b) show the normal and 1st order titration curves. The results of titration (Re%, E_r% and RSD%) are listed in Table 3-23.



(a)Titration curve of electrode B1.



(b) Titration curve of electrode B1, by using first derivative.

Figure 3-15:- (a)Titration curve of electrode B1, for 15 mL of 0.01M of iron (III) solution with 0.1 M of (NaOH) as a titrant solution, (b) Titration curve of electrode B1, by using first derivative.

Table 3-23:- Standard iron (III) solution analyses results by using titration method for electrode B1.

Titration Figure	Vol. mL at the end point	C_U(M)	Re%	RSD*%
Figure 3-15-(a)	4.5	1.000×10^{-2}	100 %	0.141%
Figure 3-15-(b)	4.6	1.002×10^{-2}	100.2 %	

RSD*% for the unknown concentration from the two figures.

3-2-6- Analyses pharmaceutical preparations via electrode (B1):-

The electrode (B1) was proved to be useful in the potentiometric determination of iron(III) in pharmaceutical preparations. The data obtained for pharmaceutical samples were listed in Table 3-24.

Table 3-24:- sample analyses of Feroglobin capsules pharmaceutical using electrode (B1).

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}
Weight(g)	0.0558	0.0558	0.0558	0.0558
Found(M)	0.999×10^{-3}	0.997×10^{-3}	0.996×10^{-3}	1.001×10^{-3}
mg/ capsule	23.975	23.979	23.961	23.970
RSD*%	0.978%	0.828%	----------	0.141 %
Re%	99.9%	99.7%	99.6%	100.1 %
E_r%	-0.1%	-0.3%	-0.4%	0.1 %
S	9.782×10^{-6}	8.264×10^{-6}	----------	----------
$\overline{x}\pm(ts/\sqrt{N})$	$0.999\times10^{-3}\pm0.122\times10^{-4}$	$0.997\times10^{-3}\pm0.102\times10^{-4}$	----------	----------

RSD*% for n=5, t=2.78

3-2-7-Comparison of iron(III) selective electrodes with another electrodes:-

Method	Membrane compenents	Linear range(M)	Detection Limit(M)	Slope (mV/decade)	pH range	Life time (day)
The proposed electrode	Fe^{+3}-chloramphenicol sodium succinate ion pair complex and di-butyl phosphate as plasticizer.	1×10^{-2}– 1×10^{-5}	9.0×10^{-6}	19.79	2.0-6.0	37
Ion selective electrode[94]	ion-pair formed between $[Fe(citrate)_2]^{3-}$ and the tricaprylylmethylammonium cation in (PVC) matrix pair and dibutylphthalate (DBPH).	1×10^{-3}-1×10^{-1}	7.5×10^{-4}	19.3	1.8-4.9	180
Ion selective electrode[95]	The membrane contain DBTS :NaTPB:NB:PVC in the ratio 2:2:64:32 for monitoring Fe^{+3}.	1×10^{-6}- 1×10^{-2}	3.6×10^{-7}	19.40	1.5- 4.7	24
Ion selective electrode[96]	Fe^{+3}- aluminum tungestate ion pair complex and dibutylphosphate as plasticizer. the composition AT: PVC: DBP in the ratio 2 : 20 : 15	1×10^{-7}- 1×10^{-1}	7×10^{-6}	20	1.0–3.5	28

3-3- Conclusions:-

The two kinds of electrodes were prepared in this study based on PVC matrix for chloramphenicol sodium succinate and iron(III).
1- Ion selective electrode for chloramphenicol sodium succinate:
ISE method included fabrication of membranes for chloramphenicol sodium

succinate was constructed based on using chloramphenicol palmitate (CPP) and sodium tetraphenylborate (TPB) as additive and many plasticizers: Di-butyl phthalate (DBPH), Di-butyl phosphate (DBP), Di-octyl phthalate (DOP), Tri-butyl phosphate (TBP) in PVC matrix membrane. The best electrode for CPSS was (A1) electrode which used to determine CPSS in the pharmaceutical sample (chloramphenicol sodium succinate injection). Also there is no interference for some interfering ion (K^{+}, Na^{+}, Fe^{+3}, Al^{+3}, Cu^{+2}, Mn^{+2}, sucrose, gelatin, CPP), it also has the working pH in the range (2.0–7.5). The practical utility of the electrode has been demonstrated by use it as indicator electrode in potentiometric precipitation titration of CPSS solution with (TPB) solution. Direct method, standard additions method and multiple standard additions method have been also successfully applied and showing a very good results. The results of these analytical methods were showed to be simple, rapid and with a good agreement in term of precision with direct method of ion selective electrode of the studied analytes by using F-test at 95% confidence interval by comparison with first derivative spectroscopy.

2- Ion selective electrode for iron(III):

ISE method included fabrication of membranes for iron(III) based on using CPSS with iron(III) as ion pair and four plasticizers; Di-butyl phthalate (DBPH); Di-butyl phosphate (DBP); Di-octyl phthalate (DOP); Tri-butyl phosphate (TBP) in PVC matrix were examined. Also there is no interference for some interfering ion (K^{+}, Na^{+}, Cu^{+2}, Mn^{+2}, Zn^{+2}, Al^{+3} and folic acid), it also has the working pH in the range (2.0-6.0). The practical utility of the electrode has been demonstrated by use it as indicator electrode in potentiometric precipitation titration of iron(III) solution with sodium

hydroxide solution. Iron(III) electrode (B1) gave good parameters by comparing with other electrodes for iron(III).

3-4-Future Work:-

Based on the above ion selective electrode studies, a future work can be applied on other ISE's which can be fabricated using:

1- Other types of drugs and antibiotic, with different properties and chemical structure, to obtain wide selectivity over drugs and multiple drugs.

2- Other methods for preparation ion exchanger (ionophore) by using silicotungstic acid ($SiO_2.12WO_3.xH_2O$).

3- Other plasticizers to get better idea on their influence on the electrode performance.

4- Other types of matrixes as alternative to PVC matrix.

5- Other physical properties of membrane: percentage of components proportions in membrane, through fixing one of the components and changing the other, and thickness by increasing the weight of the components or changing the diameter of a glass casting ring.

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1- Standard Deviation (SD)

$$SD = \frac{\sum(x_i - \bar{x})^2}{N - 1}$$

Where:

X_i = concentrations of individual deviations.

$\bar{x}$ = Mean of concentration.

N = no. of degrees of freedom.

2- Relative Standard Deviation (RSD%)

$$RSD\% = \frac{S.D}{\bar{X}} \times 100$$

3- Relative Error (E_r%)

$$E_r\% = \frac{d}{u} \times 100$$

Where:

d = Absolute Error, the difference between the measurment quantity (X_i) and the true or accepted value of the quantity (u).

4- Recovery (Re%)

$$\text{Recovery (Re) } \% = \frac{Xi}{u} \times 100$$

5- F-test

$$F = \frac{S_a^2}{S_b^2}$$

Where:

S_a, S_b are the standard diviations for first and second methods respectivily, ($S_a > S_b$). If $F_{calculate} < F_{table}$, we conclude that there is no significant difference in the precision between the two methods.

5- confidence limit for $\mu = \mathbf{X} \pm \mathbf{(ts/\sqrt{N})}$

If $t_{calculate} < t_{table}$ we accept the hypothesis lie **X=μ**

Then conclude that there is no significant difference or systematic error.

الخلاصه

في هذه الدراسة تم تحضير نوعين من الاقطاب السائلة اساسه من مادة البولي ڤاينايل كلورايد. اربعة اقطاب انتقائية للكلورامفينيكول صوديوم ساكسينيت والتي تعتمد على (Chloramphenicol palmitate)وكذلك(Sodium tetraphenylborate) كمادة مضافة مساعدة اما النوع الاخر اربعة اقطاب انتقائية للحديد(III) التي تعتمد على المعقد المحضر (Chloramphenicol sodium succinate-Iron(III)) . وبأستخدام الملدنات التالية :

- Di-butyl phthalate (DBPH)
- Di-octyl phthalate (DOP)
- Di-butyl phosphate (DBP)
- Tri-butyl phosphate (TBP)

دراسة خواص الأقطاب و التي تشمل (مدى التركيز الخطي وميل منحني المعايرة وحد التحسس وزمن الاستجابة وعمر القطب ومدى الدالة الحامضية والانتقائية) وكذلك تطبيق المعالجة الاحصائيه على هذه النتائج والتي تشمل (نسبة الانحراف القياسي ونسبة الخطأ وحد الثقة للتراكيز).من خلال هذه النتائج نلاحظ:

1- **الاقطاب** الكلورامفينيكول صوديوم ساكسينيت

CPP+TPB+DBPH (membrane A1), CPP+TPB+DBP(membraneA2), CPP+TPB+DOP (membrane A3), CPP+TPB+TBP (membrane A4),

لها **إنحدار**(48.98, 49.66 , 51.45, 53.98) **ملفولت/حقبة** ومدى التراكيز الخطي ($5x10^{-4}$-$1x10^{-1}$, $1x10^{-4}$-$1x10^{-1}$, $5x10^{-4}$-$1x10^{-1}$,$1x10^{-4}$-$1x10^{-1}$) **مولاري وحد تحسس** ($1x10^{-5}$, $3x10^{-5}$, $2x10^{-5}$, $5x10^{-5}$) **مولاري وزمن الاستجابة** (35, 20, 18, 15) ثانية لتركيز محلول 10^{-3} **مولاري** من الكلورامفينيكول صوديوم ساكسينيت. **وعمر القطب** (50,15,23, 21), يوم ومدى الدالة الحامضية وجد بحدود (2 –7.5) . و كذلك استخدم **القطب** A1 (CPP+TPB+DBPH) في التقديرات الإجهادية لتعين الكلورامفينيكول صوديوم ساكسينيت في الأدوية التجارية.

2- الاقطاب الانتقائية للحديد (III)

CPSS-Fe(III)+ DBP (membrane B1), CPSS-Fe(III)+ DBPH(membrane B2), CPSS-Fe(III)+DOP(membraneB3), CPSS-Fe(III)+TBP (membrane B4).

لها **إنحدار**(13.82, 16.01 , 26.60, 19.79) ملفولت/حقبة ومدى التراكيز الخطي ($1x10^{-5}$-$1x10^{-2}$, $1x10^{-6}$-$1x10^{-2}$, $1x10^{-5}$-$1x10^{-2}$,$1x10^{-5}$-$1x10^{-2}$) **مولاري وحد تحسس** (9×10^{-6}, 7×10^{-5}, 2×10^{-6}, 9×10^{-5}) **مولاري وزمن الاستجابة** (10, 35, 15, 30) ثانية لتركيز محلول للحديد (III) 10^{-3} **مولاري. وعمر القطب** (16, 23, 41, 37) يوم ومدى الدالة الحامضية وجد بحدود (2-6) **بأستخدام القطب** B1 (CPSS-Fe(III)+DBP). **وكذلك استخدم القطب** B1 في تعيين الحديد في الادوية التجارية .

كذلك تعيين معامل الانتقائية ($K^{pot}_{A,B}$) للاقطاب الانتقائية للمتداخلات التالية:

(Na^{+}, K^{+}, Mn^{+2}, Cu^{+2} Zn^{+2}, Fe^{+3}, Al^{+3} ,Chloramphenicol palmitate, Folic acid, Sucrose, Galaten)

بوساطة طريقة المحاليل المنفصلة وطريقة المحاليل الممزوجة.

اما طريقة الدراسات الطيفية UV- spectrophotometry تشمل:

- دراسة المشتقات الطيفية الأولى للكلورامفينيكول صوديوم ساكسينيت في (258nm) و بمعامل إرتباط يساوي (r^2=0.99925) وبتركيز خطي (2-64 **ملغرام/ لتر**).حيث تمت مقارنة نتائج الاقطاب الانتقائية مع نتائج المشتقة الاولى من خلال اجراء ال F-test حيث كانت النتائج ان طريقة الاقطاب الانتقائية هي الافضل لان نسبة القيمة العملية اقل من النظرية عند حد الثقة 95%.

جمهوريه العراق
وزاره التعليم العالي والبحث العلمي
جامعه النهرين/كليه العلوم
قسم الكيمياء

تصنيع اقطاب انتقائية جديدة لتقدير كل من الكلورامفينيكول صوديوم ساكسينيت والحديد الثلاثي وتطبيقاتها في المستحضرات الصيدلانية

رسالة
مقدمة إلى كلية العلوم - جامعة النهرين
وهي جزء من متطلبات نيل درجة الماجستير في الكيمياء

من قبل
وئام رعد عزيز
بكالوريوس كيمياء 2008 (جامعة النهرين)

تحت إشراف
أم.د. خالدة حميد محمد السعيدي

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