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Preparation of new polymeric electrodes for sulfamethoxazole and their use in determining some drugs

A Thesis Submitted to the College of Science, Al-NahrainUniversity asa Partial Fulfillment of the Requirements for the Degree of Master of Science in Chemistry

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بسم الله الرحمن الرحيم

يا آيها الناس قد جاءتكم موعظة من ربكم وشفاءٌ لما في الصدور وهدًى ورحمة للمؤمنين

الاية (57) من سورة يونس

الإهداء

الى الشمعة التي أحترقت لتنير دربي...
إلى من كلله الله بالهيبة والوقار وعلمني العطاء بدون انتظار ...
إلى من أحمل أسمه بكل افتخار...
ابي الغالي(رحمه الله تعالى)

إلى التي نذرت شبابها من اجلي...
الى التي صبرت وسهرت من اجل راحتي...
إلى من كان دعائها سر نجاحي وحنانها بلسم جراحي...

امي الغالية

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

زوجي

إلى شمسي وضياء نهاري...

ولدي

الى من تقر بهم عيني...
الى من شجعني في الشدائد...
إلى من كانوا ملاذي وملجئي...

اخوتي واخواتي

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

سراء

Summary :-

In this study two types of ion-selective electrodes (ISEs) were prepared based on PVC matrix membrane.**First**, four ion-selective electrodes for sulfamethoxazole (SMZ) which based on sulfamethoxazole (SMZ) and tungestophosphoric acid (TPA) ion-paircomplexas the electro-active materials were prepared. **Second**, six ion-selective electrodes for sulfamethoxazole (SMZ) whichbased on sulfamethoxazole (SMZ) and sodium tetraphenylborate (NaTPB) ion-paircomplex as the electro-active materials were also prepared.In both types of ISEs, some of the selectedplasticizers were used such as; Di-octyl phthalate (DOPh), Tri-butyl phthalate (TBPH), Tri-butyl phosphate (TBP),Nitrobenzene (NB), Acetophenone (AP) and o-Nitrophenyloctylether (o-NPhOE) in PVC matrix.The electrodes parameters, linear range of concentration,Nernestian slope, limit of detection, response time, life time, working pHrang and selectivity were evaluated. Also the statistical treatments wereapplied for the results that include: relative standard deviation (RSD),relative error (Re.), and confidence limit for concentration. The results showed:

The first type ISEs were: SMZ-TPA+DOPH (E1),SMZ-TPA+TBP (E2),SMZ-TPB+AP (E3) andSMZ-TPA+NB (E4), give the linear Range from (1×10^{-5}-1×10^{-2}, 1×10^{-7}-1×10^{-2}, 1×10^{-5}-1×10^{-2} and 1×10^{-5}-1×10^{-2} M), and the slopes are (52.008, 58.381, 56.909 and 50.309 mV/decade)respectively, with detection limits are (9×10^{-6}, 9×10^{-8}, 6×10^{-6} and 7×10^{-6}M), response time of 10^{-3} M (30, 28, 36 and 25 second) and the lifetimewere about (29, 27, 20 and 9 days) respectively.

The second type, were: SMZ-NaTPB+TBPH (L1), SMZ-NaTPB +NB (L2), SMZ-NaTPB +TBP (L3), SMZ-NaTPB +AP (L4),SMZ-NaTPB +DOPH (L5) and SMZ-NaTPB +o-NPhOE (L6) give the linear range

from (1×10^{-5}-1×10^{-2}, 1×10^{-5}-1×10^{-2}, 1×10^{-5}-1×10^{-2}, 1×10^{-5}-1×10^{-2}, 1×10^{-5}-1×10^{-2} and 1×10^{-5}-1×10^{-2}M), the slopes are (53.609, 49.608, 56.810, 55.709, 50.808 and 51.808 mV/decade)respectively, with detection limits of (9×10^{-6}, 8.5×10^{-6}, 8×10^{-6},8.9×10^{-6}, 7.5×10^{-6} and 7×10^{-6}M), response time of 10^{-3} M (16, 14, 24, 19, 16 and 20 second) and the lifetime were about (12, 6, 24, 17, 26 and 7 days) respectively.

The best electrode from first kind is (E2) and from the second kind is (L3), both were used to determine the sulfamethoxazole in pure samples. The working pH for (E2) electrode was ranged from (1.6-6.8) and the working pH for (L3) electrode was ranged from (1.7-6.9). The interferences measurements in the presence of (Na^{+}, K^{+}, Cu^{+2}, Mn^{+2}, Fe^{+3}, Al^{+3}, trimethoprim, starch, sucrose and gelatin) were studied for both electrodes using the separated method and mixed method for selectivity coefficient determination.

The ISE (E2) gave a good electrochemical characterizationamong the others and it has been used successfully for the determination ofsulfamethoxazole in the Pharmaceutical Samplesusing different potentiometricmethods.

Also UV-spectrophotometric method was used which include the normal spectra,forsulfamethoxazole solutions ($0.990x10^{-4}$, $0.996x10^{-4}$,$0.999x10^{-4}$, $1.004x10^{-4}$, $1.005x10^{-4}$)M in wavelengthequal 259.00 nm. The analytical methods results showed to be simple, rapid and with a good accuracy by comparing between normalspectra and direct method of Ion selective electrode by using F-test.The results shown, that the sulfamethoxazole canbe 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 less than F-table, we concluded that there is no difference in precision between two methods.

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List of abbreviation

SMZ	*Sulfamethoxazole*
TBP	*Tributylphosphate*
DOPH	*Dioctylphthalate*
NB	*Nitrobenzene*
TBPH	*Tributylphthalate*
AP	*Acetophenone*
ONPOE	*O-nitrophenyloctylether*
TPA	*Tungestophosphoric acid*
NaTPB	*Sodiumtetraphenylborate*
THF	Tetrahydrofuran
Erel.	Relative error
ISE	Ion-selective electrode
F.W.	Formula weight
FIM	Fixed interference method
CST	*stock unit of viscosity gm/sec.cm.density*
e.m.f	Electromotive force
FPM	Fixed primary ion method
FTIR	Fourier transform infrared spectroscopy
HPLC	High performance liquid chromatography
LC	liquid chromatography
MPM	Match potential method
TSM	Two solution method
MSA	Multi Standard addition method
mV	Millivolt
PVC	Poly vinyl chloride
Rec.	Recovery
RSD	Relative standard deviation
δn_{-1}	Standard deviation
SAM	Standard addition method
SCE	Saturated calomel electrode
SHE	Standard hydrogen electrode
Std.	Standard

Introduction

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

An ion-selective electrode (ISE) is a sensor, which are part of a group of relatively simple and inexpensive analytical tools, based on thin films or selective membranes as recognition elements that converts the activity of a specific ion dissolved in a solution into an electrical potential, which can be measured by a voltmeter or pH meter as shown in figure (1-1). ISE is an electrochemical half-cell equivalent to other half-cells of thedifferent kinds. These devices are distinct from systems that involve redox reactions, although they often contain a secondkindelectrodeastheinternal reference electrode. The ion selective electrodes must be used in conjunction with a reference electrode (i.e. externalreference electrode) to form a complete electrochemical cell. The measured potential differences (ISE versus outer reference electrode potentials) arelinearlydependent onthelogarithmoftheionic activity,accordingtotheNernstequation[1].The pH electrodeis animportant electrode of this group because its standard potentialis set at 0, and all other electrodes' standard potentials are measured with respect to it[2].

1-2-Ion selective electrode cell measurements:-

The cell consists of both an indicator and reference electrode. Since the potential of the reference electrode is constant, the potential developed at the indicator electrode that contains information about the amount (activity) of analyte in a sample.An electrochemical sensor based on a thin selective membrane or film as recognition element is an electrochemical half-cell equivalent to other half-cells of the different kinds. The components of electrochemical cell are shown in Figure 1-1. The potential developed at the membrane is the result of either an ion

exchange process or an ion transport process occurring at each interface between the membrane and solution.

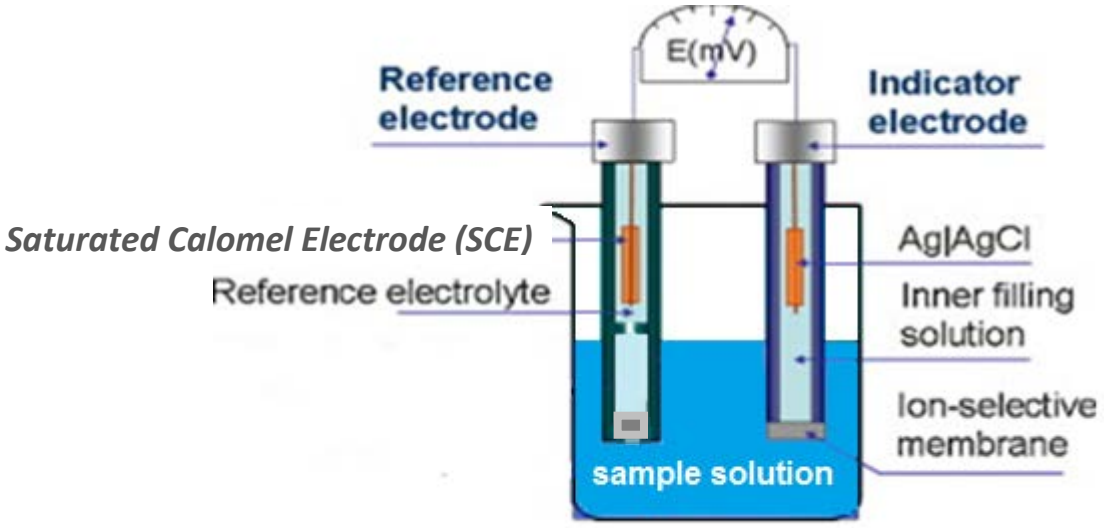


Figure 1-1:- A classical ion selective electrode in electrochemical cell[3].

Generally, the cell contains two reference electrodes, "internal" and "external", and a selective membrane as the recognition element. However, besides this conventional type of the cell with solution contact on both sides of the membrane there are ISE cell arrangements with wire contact to one side of the membrane. Conventional notation of the cell is[3]**:-**

External ref. │ test solution │ membrane │internal ref.

The measured cell e.m.f, E is described with the Nernst equation[4]**:-**

$$E = E^0 - (RT/nF) \ln a \quad \ldots 1\text{-}1$$

$$E = E^0 - (2.303RT/nF) \log a \quad \ldots 1\text{-}2$$

Where E^0 = constant for a given cell, E = the total potential developed between the sensing and reference electrode (mV), R = gas constant (8.314 joule $mole^{-1}deg^{-1}$),T= temperature in Kelvin (298ºK or 25^0C), n = ionic charge, F = faraday constant(96485 coulombs), a = is the ion activity. At room temperature (25^0C) Nernst equation is frequently expressed as:-

$$\mathbf{E_{(mV)} = E^0 - (59.2 / n) \log a} \qquad \textbf{…1-3}$$

Cell design according to the basic rule of designing of electrolytical cells, with a condition that the current passed through the electrolytical cell equals zero, as showed in Figure 1-1. The exchange that occurs between the internal and external solution across the membrane depends on ionic exchange and the active ionophore which used in the membrane[5].

$$\mathbf{E_{total} = E^0 + E_{junction} – E_{membren}} \qquad \textbf{…1-4}$$

1-3- The advantages of (ISEs) [6]:-

1- Ion-SelectiveElectrodesarerelatively inexpensive andsimple touse and have an extremely wide range of applications and wide concentration range.2- They are unaffected by sample color or turbidity.

3- The mostrecent plastic-bodied all-solid-state or gel-filled models are very strong and permanent and ideal for use in either field or laboratory environments.

4- They are particularly useful in biological applications because they measure the activity of the ion directly, rather than the concentration.

5- In applications where interfering ions, pH levels, orhigh concentrations are a problem, then many manufacturers can supply a library of specialized experimental methods and special reagents to overcome manyofthese difficulties.

6- With careful use, frequent calibration, and an awareness of the limitations, they can achieve accuracy and precision levels of ±2 or 3%for some ions and thus compare favorably with analytical techniques which require far more complex and expensive instrumentation.

7- ISEs areoneof thefewtechniques which can measure both positiveandnegative ions.

8- ISEs can be used in aqueous solutions over a wide temperature range.Crystal membranes can operate in the range 0° C to 80° C and plastic membranes from 0° C to 50° C.

1-4-Limitation in ISE measurements:-

1-4-1-Diffusion:-

Orion Research points outthatdifferenceinthe ratesofdiffusionofionsbased on size can lead to some error.In theexample of sodium iodide, sodium diffuses across the junction at a given rate. Iodide moves much slower due to its larger size. Tocompensateforthistype it is important that a positive flow of fillingsolution move through the junction[6].

1-4-2-Sample ionic strength:-

The total ionic strength of a sample affects the activity coefficient andthat itisimportantthat this factorstayconstant. [7].This adjustmentislarge, comparedto the ionic strength of the sample, such that variation between samplesbecomes small and the potential for error is reduced[8].

1-4-3- Temperature:-

Itisimportant thattemperaturebecontrolledas variation in this parameter Canlead tosignificant measurementerrors[7].A singledegree (C) changeIn sampletemperaturecanleadtomeasurement errors greater than 4%[9].

1-4-4- pH:-

Some samples may require conversion of the analyte to one form by adjusting the pH of the solution[6]. Failure to adjust the pH in these instances can lead to significant measurement errors[10].

1-4-5-Interferences:-

The background matrix can affect the accuracy of measurements taken using ISE's[6]. Covington was pointed out that some interference may be eliminated by reacting the interfering ions prior to analysis[10].

1-5- The applications of ISEs:-

1-5-1- Agriculture:-

Determination of nitrate, potassium, calcium and chloride in soils[11].Measurement of nitrate content of fertilizers[12].

1-5-2- clinical laboratories:-

Determination of various species including calcium, potassium, chloride in serum, blood, plasma and other body fluids [13]. Analysis of fluoride in skeletal structures and Investigation of fluoride in dental studies[14].

1-5-3- pulp:-

Analysis of chloride in pulping liquors[6].

1-5-4- Pollution monitoring:-

Levels of cyanide, fluoride, sulphide and chloride can be measured ineffluents, natural waters and waste-matters[15]. The use of electrodes forcontinuous and trouble-free monitoring makes them increasingly suitable for pollution monitoring [16].

1-5-5- Detergent manufacture:-

The measurements of calcium and barium can be used to study the effects of detergents on water quality[17].

1-5-6- Education and research:-

Electrodes of all types arebeing used as sensors in many experiments tostudy reaction mechanisms, equilibria, activitycoefficientsandsolubility,electrodes are simple and inexpensive enough to be used byundergraduates as part of analytical chemistry training, electrodes are particularlysuitable fornuclear applications sincethey areunaffected by radiation. Fluoridefinds wideapplication infuelreprocessingsolutions[17].

1-5-7- Explosives:-

Fluoride, chlorideandnitrate havebeenmeasuredinexplosives andtheir combustionproducts[6].

1-5-8- Food processing:-

Determinationof salt content of meat, fish, milk,fruit juices and beer.Analysis of fluoride in drinking water, mineral drinks, fish protein, tea,beer, measurement of calcium in milk and beer[6].Determination of potassium in fruit juices and wine-making[18].

1-6-Applications of ISEs in pharmaceutical drugs and ions:-

Theionselective membranes are widely used for pharmaceutical analysis with advantages of determining sample directly, rapidly and simplicity.Table shows some applications of ion selective electrodes in pharmaceutical drugs and ions.

1-7- Classification of membrane selective electrode depend on physical and chemical nature of the active material from which the membrane is made:-

1-7-1- Primary ion selective electrodes:

1-7-1-1- Crystalline electrodes[1]:

May be homogeneous or heterogeneous:

(a) Homogeneous membrane electrodes are ion-selective electrodes in which the membrane is a crystalline material prepared from either asingle compound or a homogeneous mixture of compounds (i.e., Ag_2S,AgI + Ag_2S**).**

(b) Heterogeneous membrane electrodes are formed when an activesubstance or mixture of active substances, is mixed with an inert matrix,such as silicone rubber or polyvinyl chloride (PVC), to form the sensingmembrane**.**

1-7-1-2- Non-crystalline electrodes:

In these electrodes, the ion-selective membrane consists of a matrix containing an ion-exchanger [see (a) and (b) below) and is usually interposed between two aqueous solutions. The matrix may be porous (e.g., cellulose ester)or nonporous (e.g., glass or inert polymeric material such as PVC)[37].

(a) Glass electrodes:

Are ion-selective electrodes in which the sensing membrane is a thin piece of special glass. The chemical composition of the glass determines the selectivity of the membrane. In this group are[37]:

(i) hydrogen ion-selective electrodes,

(ii) monovalentcation-selective electrodes.

A common form of the glass membrane electrode is depicted in Fig. 1-2. In use for measurement of pH, the glass membrane separates two liquid phases. One is

inside the electrode as shown and it is typically 0.1 F hydrochloric acid.The other is the test solution into which the electrode is dipped. Two referenceelectrodes are employed, one in each of the two solutions.The difference in potential between the two reference electrodes ismeasured by means of an electronic voltmeter.A typical modern pH probe is a combination electrode, which combines both the glass and reference electrodes into one body. The combination electrode consists of the following parts (see the drawing**):**

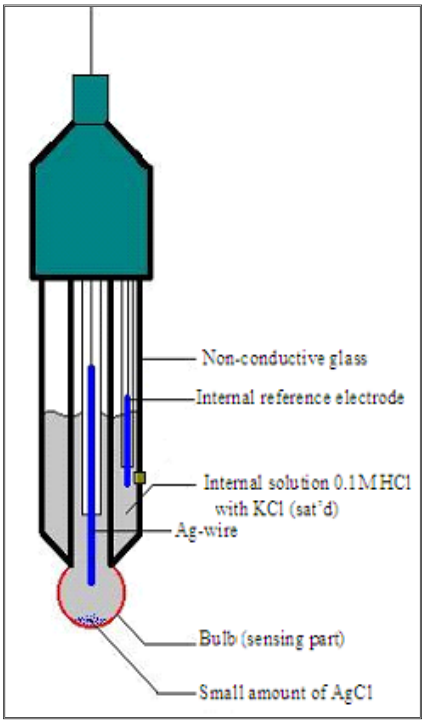


Figure 1-2: A glass pH electrode[37].

The bottom of a pH electrode balloons out into a round thin glass bulb. The pH electrode is best thought of as a tube within a tube. The innermost tube (the inner tube) contains an unchanging 1×10^{-7}mol/L HCl solution. Also inside the inner tube is the cathode terminus of the reference probe. The anodic terminus wraps itself around the outside of the inner tube and ends with the same sort of reference

probe as was on the inside of the inner tube. It is filled with a reference solution of 0.1 mol/L KCl and has contact with the solution on the outside of the pH probe by way of a porous plug that serves as a salt bridge[38].

(b) Electrodes with mobile charged sites[39]:

(i) ***Positively charged hydrophobic cations:***- (for example quaternary ammonium salts) which dissolved in a suitable organic solvent and held in an inert support (for example poly(propylene carbonate) filter or PVC), provide membranes which are sensitive to changes in the activities of anions**.**

(ii)*Negatively charged hydrophobic anions:*- (for example tetra-chlorophenylborate) which dissolved in a suitable organic solvent and held in an inert support (for example poly(propy1ene carbonate) filter or PVC), provide membranes which are sensitive to changes in the activities of cations.

(iii) ***Uncharged 'carrier' electrodes***

based on solutions of molecularcomplexingagents of cations (for example antibiotics) and anions which can be used in ion exchanger membrane preparations to give sensitivity and selectivity to certain cations and anions**.**

(iv) hydrophobic ion-pair in plasticized PVC -containing a dissolved hydrophobic ion pair (for example cationic drug as cationtetraphenylborate or anionic drug as tetra-alkylammonium salt of an anion) responds to component ion activities in bathing electrolytes**.**

1-7-1-3-Molecularly imprinted sensor :-

Molecular imprintingsensor is a high selectivesensor which provide synthetic receptors capable of recognizing traces ofanalytesin biofluids like blood, urine etc. It involvesself assembledcomplexationof a substrateto functionalmonomers to form a polymer complex[40].

1-7-2- Multiple membrane (multilayer) ion selective electrodes:-

1-7-2-1Gas sensing electrodes:-

Gas sensing electrodes as shown in Figure 1-3; respond to dissolved gases in solution. They have a plastic body that is usually made of polytetrafluorethylene. The dissolved gas diffuses across the membrane into a small volume of buffer. The reaction of the gas with the buffer causes a pH change which is sensed by an internal glass pH electrode. Carbon dioxide and ammonia are among the species measured by gas sensing electrodes[41].

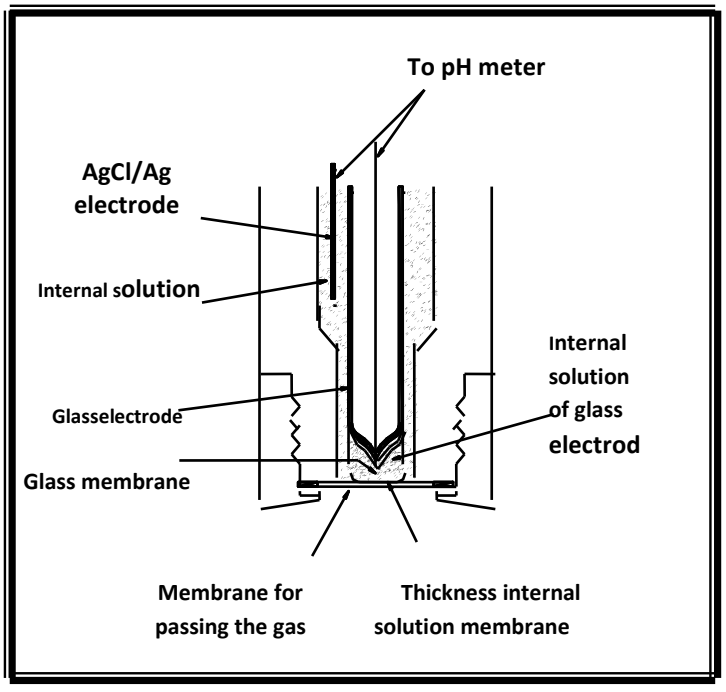


Figure (1- 3):- A gas sensing electrodes type [42].

1-7-2-2-Enzyme electrodes:-

Enzyme electrodes definitely arenot true ion selective electrodes but usually are considered within the ion specific electrode topic. Such an electrode has a double reaction mechanism, an enzyme reacts with a specific substance, and the product of this reaction(usually ammonia or carbon dioxide) is detected by a true ion selective electrode, such as a pH selective electrode. All these reactions occur inside a special membrane which covers the true ion selective electrode.An example isglucose selective electrodes [43].

1-8-Reference electrodes:-

Reference electrodes are applicable in instances where the electrical potentialis to be measured in a solution. Also, it has a stable and well defined electrochemical potential against which the applied or measuredpotentials in an electrochemical cell are referred, Reference electrode is necessary to complete electrochemical cell. It is preferable to use a double junctionreference electrode for ISE applications. Standard reference half cells haveKCl based electrolyte filling solutions, as shown in Fig. 1-4. This is a distinct disadvantage when, for example,potassium or chloride is beingmeasured. To overcome this, a double junction reference is used in which theescaping KCI is retained in a second chamber containing a non-interfering electrolyte, which in turn escapes into the test solution at the second junction

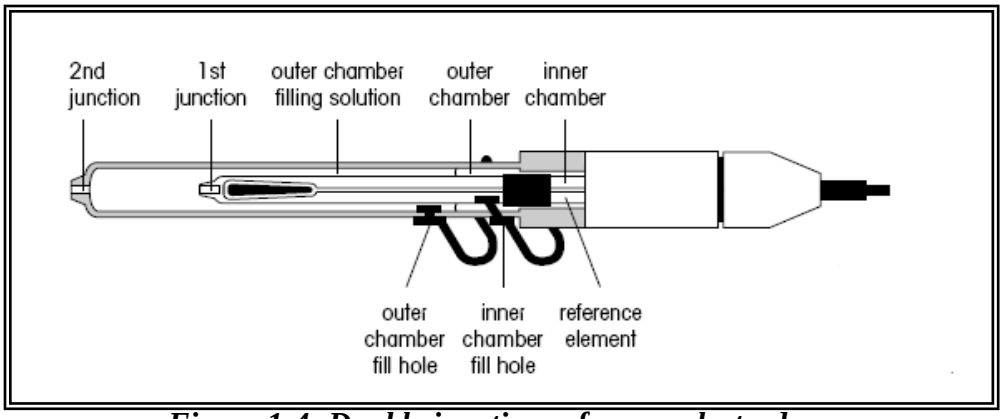


Figure 1-4: Double junction reference electrode.

Mostly electrodes of the second kind are used as reference electrodes. On account of its environmental compatibility, the Ag/AgCl/Cl^{-1}electrode is preferably used. The $Hg/Hg_2Cl_2/Cl^{-1}$ (calomel) electrode, introduced by Ostwald as early as1894, has advantages with regard to potential stability but it is only applicable up to temperatures of about 80 °C. This electrode is commercially available, while, in contrast, the Tl(Hg)/TlCl/Cl^{-1}system, the Thalamid electrode, has been banned because of its toxicity [44].

1-9-Characterization of ISEs:-

1-9-1-Calibration curve:-

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 (RE) immersed in the same solution, and the logarithm of the activity of the ions in the solution[45]. This relationship is described by the Nernst equation:

$$\mathbf{E = constant \pm (2.303\ RT/\ nF) \log a} \qquad \mathbf{...1\text{-}5}$$

Figure 1-5 shows, a typical plot of the electrochemical cell (i.e. the potential difference measured between the ISE and the external RE of a given ion-selective electrode cell assembly) versus the logarithm of the single ionic activity (concentration) of a given species.

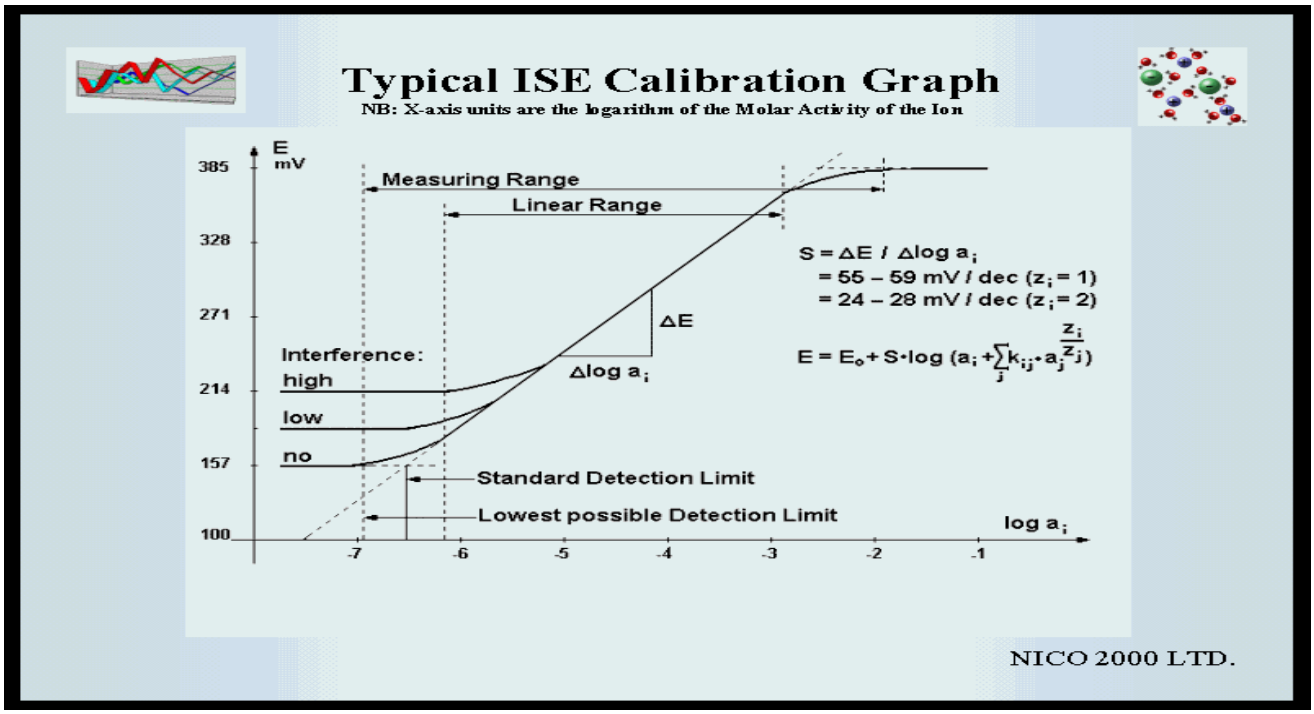


***Figure 1-5:- Typical ISE calibration graph*[46].**

It is recommended that theelectrochemical cell is ascribed to the ordinate (vertical axis) with the more positive potentials at the top of the graph and that pa_A (-log activity of the measured species A) or pc_A (-log concentration of the measured species A) is ascribed to the (horizontal axis) with increasing activity or concentration to the right[1].The linear rang is a part of the calibration curve through which a linear regression would demonstrate that the datapoints do not deviate from linearity by more than 2 mV[47].

1-9-2-Slope:-

The magnitude 2.303RT/nF from equation 1-5, is the slope of the line (from the straight line plot of E versus log a, which is the basis of ion selective electrode calibration graphs) as shown in Figure 1-6. The theoretical value for the slope at 25 ^{0}C is 59.2 for monovalent ions, 29.6 for divalent ions and 19.7 for trivalent ions. The slope is usually measured in unit of mV/decade[6]. The slope gets lower with passing time because of the electrode contamination, and the low slope means that the higher errors in the sample measurements [48].

1-9-3-Detection limit:-

According to the IUPAC recommendation [7], the detection limit is defined by the intersection of the two extrapolated linear parts of the ion selective calibration curve as shown in Figure 1-6. The observed detection limit is often governed by the presence of other interfering ions and the purity of standard solutions used for calibration curve.

1-9-4-linear Range of concentration:-

The linear rang of concentration is a part of the calibration curve (Figure 1-6) through which a linear regression would demonstrate that the data points do not deviate from linearity by more than ±2 mV. Typically, the electrode calibration curve exhibits linear response range between 10^{-7}M and 10^{-2}M[49].

1-9-5-Stability and lifetime:-

The stability and lifetime are features associated with the response behavior of ISEs[5]. They include the same factors which influence the response time (solution concentration, the interfering ions, which poison the electrode surface). 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 lifetime[49].

1-9-6-Response time[50]:-

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 and the first instant at which the potential of the cell becomes equal to its steady-state value within ±1mV for the final equilibrium potential. Generally electrodes with liquid ion-exchanger membrane have longer response time than solid membraneelectrode. This may be due to the slow rate of reaction between the determined ion and the ion-exchanger which lead to slower transport of the ions across the membrane-solution interface. However, the main factors that influenced on the response time include; the type of membraneand the presence of interferences which all slow the response time of these electrodes**.**

1-9-7- Selectivity:-

Selectivity of ion selective electrodes is quantitatively related to equilibriaat the interface between the sample and the electrode membrane[51]**.** Moreover, they are also required for theoptimization ofionophore structures and membrane compositions. For example, errors arise when the response to a weakly interfering ion is also influenced by the primary ion leaching from the membrane.

A detailed to determine correct potentiometric selectivitycoefficients unaffected by such biases is presented. The potentiometricselectivity coefficient is expressed according to the Nicolsky-Eisenman equationas:

$$\mathbf{E = E_0 + R\,T / Z_A F \ln [a_A + \Sigma K_{A,B}(a_B)^{Za/Z_b}] \ldots 1\text{-}6}$$

Where E is the measured potential; E_0 is a constant that includes thestandard potential of the electrode, the reference electrode potential, (z_A, z_B, $a_A$and $a_B$are the charge numbers and activities of theprimary ion, A, and the interfering ion, B respectively); and $K_{A,B}$is thepotentiometric selectivity coefficient for the primary ion A against theinterfering ion B. This selectivity coefficient can be determined using eitherseparate solutions or match solutions method, containing both the analyteA,and the interfering B ions. Potentiometric selectivity coefficients can bemeasured with different methods that fallinto two main groups[52]:

1-9-1-1- Separate solution methods:-

1-9-1-1-1- When ($a_A = a_B$)[53]:-

The potential of a cell comprising an ion selective electrode and a reference electrode is measured with two separate solutions, one containingthe ion A at the activitya_A(but no B), the other one containing the ion B at the same activity $a_A = a_B$(but no A). If the measured values are E_A and E_B, respectively, the value of$K_{potA,B}$is calculated from the equation:

$$\mathbf{\log K_{potA,B} = (E_B - E_A)\, Z_A F / R\,T \ln 10 + (1 - z_A/z_B) \log a_A \ldots 1\text{-}7}$$

or for any electrode in general, where ($Z_A F / R\,T \ln 10$) =1/S

$$\mathbf{\log K_{potA,B} = (E_B - E_A) / S + (1 - z_A/z_B) \log a_A \ldots 1\text{-}8}$$

Where (S) is the slope of the electrode.This method is recommended only ifthe electrode exhibitsa Nernstian response. It isless desirablebecause it does not represent as well the actual conditions under which the electrodes are used**.**

1-9-1-1-2- When ($E_A = E_B$)[54]*:-*

The potential of an ISE for the primary and interfering ions are obtained independently. Then, the activities that correspond to the same electrodepotential value are used to determine the $K_{potA,B}$value and it equal**:**

$$K_{potA,B} = a_A / (a_B)^{Za/Zb} \ldots 1\text{-}9$$

1-9-1-2- Mixed solution methods:-

1-9-1-2-1- Fixed interference methods (FIM) [55,56]*:-*

The potential of a cell comprising an ion selective electrode and a referenceelectrode ismeasured with solutions of constant level of interference, a_B, and

varyingactivity of the primary ion, a_A.**:**

The potential values obtained areplotted vs the activity of the primary ion as shown in Fig. 1-6. The intersection of the extrapolation of the leaner portions of this curve will indicate the values of $a_A$which are to be used to calculate $K_{potA,B}$from the equation**1-9.**

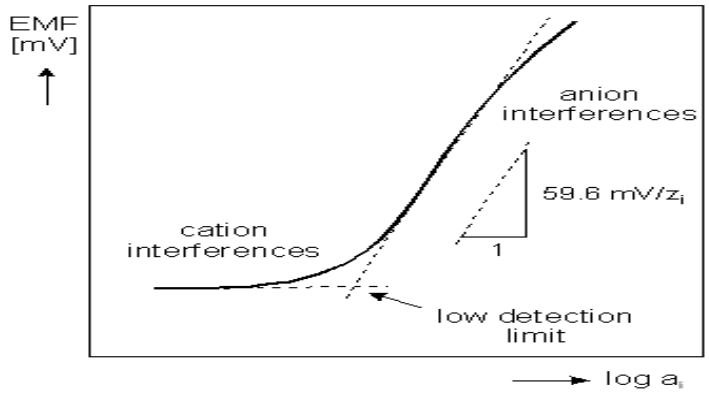


Figure 1-6:- Determination of $a_A$value according to FIM [57]**.**

1-9-1-2-2- Fixed primary ion method (FPM) [58,59]:-

Thee.m.f of the cell comprising andaion selective electrode and reference Electrode (ISE cell) is measured for solutions of constant activity of the primary ion, $a_A$and a varying activity of the interfering ion, a_B**..** The e.m.f. values obtainedare plotted vs. the logarithm of the activity of the interfering ion. The intersection of the extrapolated linear portions of this plot indicates the value of $a_B$that is to be used to calculate $K_{potA,B}$ from the equation 1-9**.**

1-9-1-2-3- Two solutions method (TSM)[58,60]*:-*

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$K_{potA,B}$is calculated by inserting the value of the potential difference, $\Delta E=E_{A+B}-E_A$, into the following equation:

$$\mathbf{K_{potA,B}= a_A \left(e^{\Delta E z_a F}/ (R\ T) - 1\right) / (a_B)^{z_a/z_b} ... \ 1\text{-}10}$$

Where z_A, z_B; and a_A, $a_{b,}$ are the charge numbers, and activities for the mixed solution.

1-9-1-2-4- Matched potential method (MPM) [61]*:-*

A theory is presented that describes the matched potential method (MPM) forthe determination of the potentiometric selectivity coefficients $K_{potA,B}$ of ion selectiveelectrodes when the charge of the primary ion not equal to charge ofinterfering ions and used in case no possible to achieve Nernstain responses for a given interfering ion. This method is based on electrical diffuse layers on both themembrane and the aqueous side of the interface.

A solutionof the primary ion Awith a fixed activity is used as the reference solution**..** 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 Fig. 1-7, another curve, I_{A+B}, is obtained from the potential change by stepwise adding the interferingion B to thereference solution

with the samecomposition as on curve I_A.When the change in potential (ΔE) on curve $I_A$ata′$_A$matches thaton curve I_{A+B} at a_{A+B}, the ratio between the activities of the primaryion A relative to the interfering ion B denotes the selectivity coefficient $K_{potA,B}$.The selectivity coefficient $K_{potA,B}$is thus obtained as

$K_{potA,B} = \Delta a_A / a_B$… 1-11

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

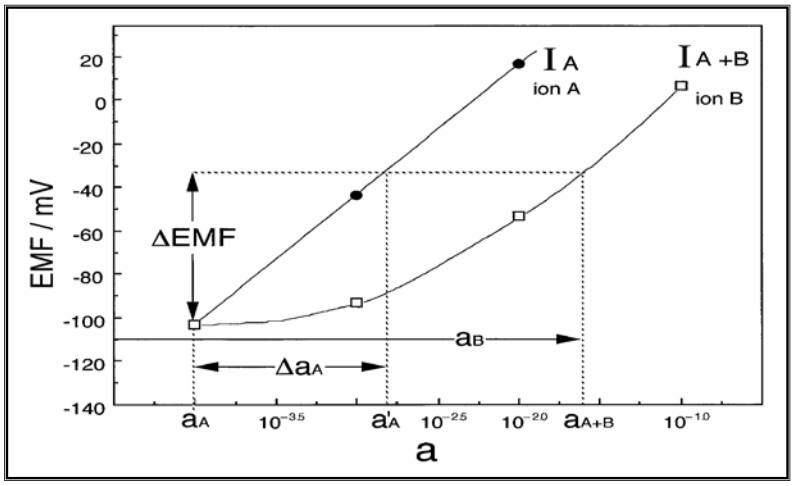


Figure 1-7:- Determination of selectivity coefficients by the matched potential method[61].

1-10-Measurement techniques:-

Many measurement techniques are based on ion selective electrodes have been described. The most important and widely used techniques for such studies are; direct method, incremental methods and potentiometric titration method**[46].**

1-10-1-Direct potentiometrymethod:-

Direct potentiometric method is the simplest and most widely used for the quantitative measurements using 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 singlecycle. Each single cycle corresponds to an order of magnitude or decade, or by usingspecial

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 and make any complicated calculations[62].

1-10-2-Incremental methods:-

1-10-2-1-Standard additions method (SAM)[62, 63]:-

This method is generally more accurate than the direct method for concentration measuring in the sample, but it is more time-consuming because of the calibration involved. In this method, the ISE cell assembly is immersed in the sample and the equilibrium cell potential is recorded, then a known volume of a standard solution of the determinant is added to the first volume and the electrode potential is re-measured, from which the potential difference (ΔE) is foundby solving the following equation the unknown concentration can be obtained:

$$C_U = C_S / 10^{\Delta E/S} [1+ (V_U / V_S)] - (V_U / V_S) \quad \ldots 1\text{-}12$$

Where C_U: the concentration of unknown solution, C_S: the concentration of standard solution, V_U: the volume of unknown solution, V_S: the volume of standard solution and S: the slope of electrode. Standard addition can be applied to most analytical techniques and is used instead of a calibration curve to solve the matrix effect problem. The standard solution is added to the unknown solution so any impurities in the unknown are accounted for in the calibration.

1-10-2-2-Multiple standard additions method (MSA)[64]:-

It is an extension of standard additions method. The response of ISE to certain analyte A, in solution free from interfering ions can be represented by Nernst equation:

$$\mathbf{E= E^0 + S\ Log\ a_A \times V_S / V_U} \qquad \textbf{...1-13}$$

Where S is the slope of the electrode, V_S, V_U, are the volumes of added standard and unknown (sample) respectively; V_U is usually set to be hundred times more than V_S. Rearranging of equation and taking the antilog gives:

$$\mathbf{Antilog\ E/S = constant \times a_A V_S / V_U} \qquad \textbf{...1-14}$$

Where antilog E/S is constant thus the antilog E/S is proportional to V_S. A plot of antilog E/S as a measure of a_A along the ordinate against $V_S$yields a straight line which can be extrapolated back to an intercept on the standard volume. The concentration of sample (unknown) can be calculated:

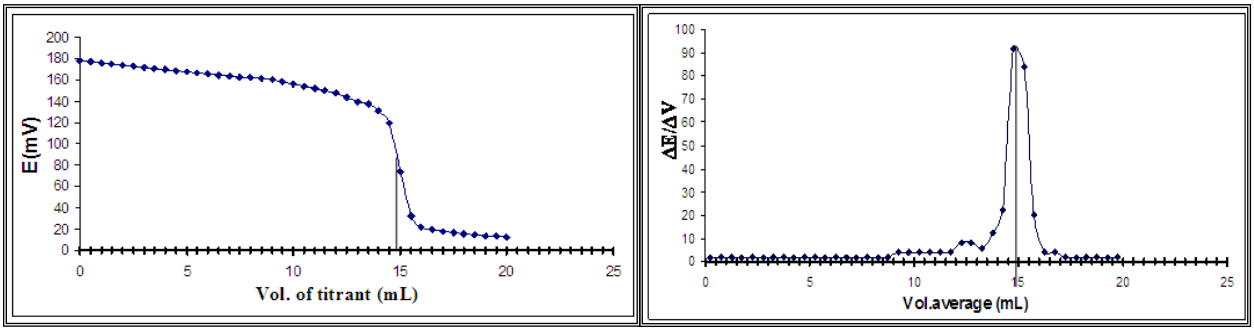
$$\mathbf{C_U = V_S \times C_S / V_U} \qquad \textbf{…1-15}$$

Where C_U and C_S are the concentration of unknown and standard, respectively, $V_S$is the volume of standard.

1-10-3-Potentiometric titration method[65]:-

Potentiometric titration method has also been used for the evaluation of the performance of ion selective electrode in which the ion selective electrode is only used as an indicator and the accuracy is derived from the classical titration process can yield answers to within 0.1-0.5%. Potentiometryis generally valuable as a technique for detecting the end-point of titrations where there is often a

change in the concentration of the reactants and thus a big shift in the electrode potential. These end point determinations can often be made more precisely than other ISE methods because they depend on the accuracy of the volumetric measurements rather than the measurement of the electrode potential. The sample is titrated with a suitable titrant and the increase or decrease in titrant activity is followed with an ISE response, to locate the equivalence point as in Figure 1-8.



a)-Titration curve. (b)-Titration curve by using first derivative.

Figure 1-8:- Potentiometric titration curves by using ion-selective electrodes: (a)-titration curve, (b)-by using first derivative [66].

1-11-Sulfamethoxazole:-

Sulfamethoxazole (**SMZ**) Sulfamethoxazole,4-Amino-*N*-(5-methylisoxazol-3-yl)-benzenesulfonamidewhich has theempirical formula ($C_{10}H_{11}N_3O_3S$),as shown in Fig. (1 - 9), is white or almost white, crystalline powder withmolecularweight253.279 g/mol,practically insoluble inwater, freely soluble in acetone, sparingly soluble in ethanol .It dissolves in dilute solutions of sodium hydroxide and in dilute acids.

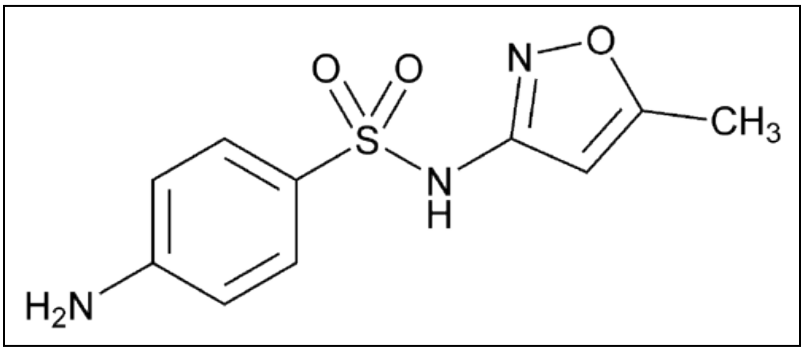


Figure 1 - 9:- Structure formula of sulfamethoxazole

Sulfamethoxazoleis mostoften used as part of a synergistic combination withtrimethoprim in a 5:1 ratio inco-trimoxazole, also known undertrade namessuch as Bactrim,Septrin, orSeptra,inEastern Europe it is marketed as Biseptol. Its primary activityis against susceptible forms ofStreptococcus, StaphylococcusaureusandEscherichia coli. It iscommonly used to treat urinary tractinfections.In addition it can be used as an alternative to amoxicillin-based antibiotics totreat sinusitis.[67]

1-12-Analyses of Sulfamethoxazole*:-*

Potentiometricmembrane sensors are playing an important role in pharmaceutical analyses because of their simplicity,rapidity and accuracy over some other analytical methods. Table 1-3; show somemethods for the analyses ofsulfamethoxazole.

1-11- Spectrophotometric method:-

Ultraviolent-visible spectrophotometer investigates theinteraction of light radiationwith matter in the ultra violet(200-400) and visible (400-800) range[72].The radiationof UVhas sufficient energy to excite valanceelectrons inmany atoms or molecules from their ground state to higher energy levels. The excited electrons transfer from a bondingto an anti-bonding orbital. [73].

Thetypical applications of UV absorption spectroscopy as shown in fig.(1-10)include the determination of poly nuclear aromatic compounds such as painting materials, vitamins, drugs and there arevariousapplications ofvisible spectrophotometric methods have been developed for analysis of different colored metal complexes and colored compounds[74].

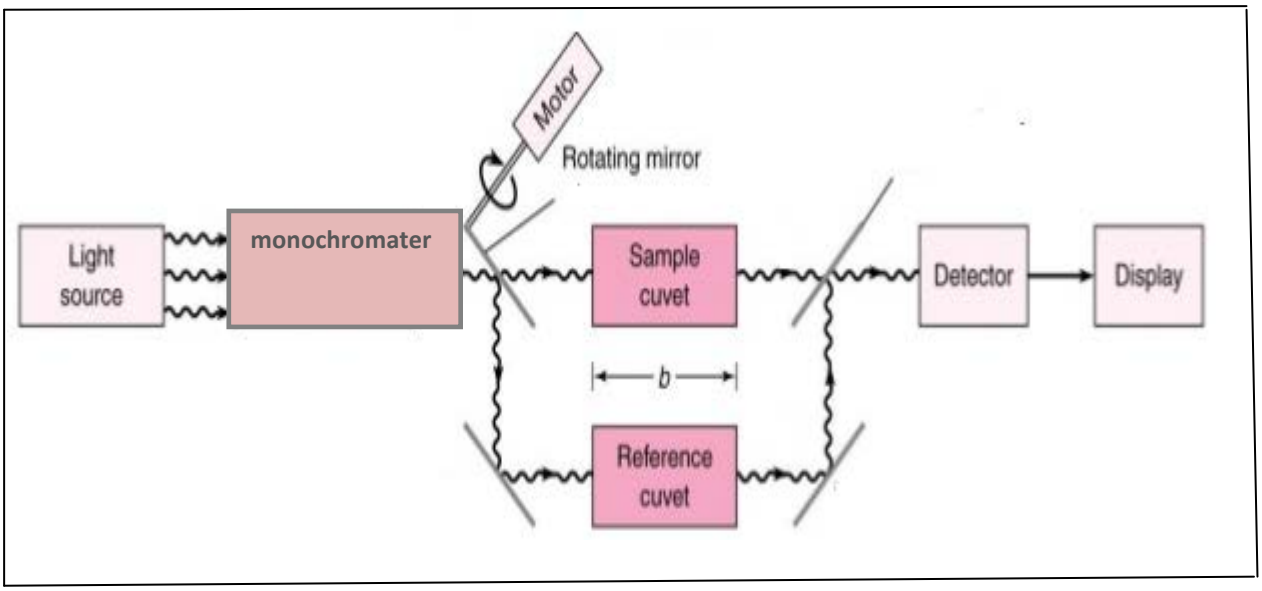


Figure 1 - 10 :- UVabsorption spectroscopy diagram[73].

1-14-Aim of the work:-

In this study two types of electrodes were prepared based on PVC matrix to determinesulfamethoxazoleinpure and pharmaceuticals form.the first type included fabrication of membranes for sulfamethoxazole(SMZ) was constructed by sulfamethoxazole with tungestophosphoric acid and many plasticizers: Tri-butylephthalatr (TBPH),o-Nitrophenyleoctyle ether (ONPOE), Di-octyl phthalate (DOPH), Tri-butyl phosphate (TBP) , Acetophenone (AP) and Nitrobenzene (NB) in PVC matrix membrane, and the second type included fabrication of membranes for sulfamethoxazole(SMZ) was constructed by sulfamethoxazole with sodium tetraphenyl borate with the sameplasticizers. Thebest electrode from the two types was (E2) electrode which used to determine sulfamethoxazole in thepharmaceutical sample.Also there is no interferences measurements in the presence of (Na^{+}, K^{+}, Cu^{+2}, Mn^{+2}, Fe^{+3}, Al^{+3}, trimethoprim, starch, sucrose and gelatin).Italso has the working pH in the range (1.6–6.8). The practical utility of the electrode has been demonstrated by use it asindicator electrode in potentiometric precipitation titration of sulfamethoxazolesolution with tungestophosphoric acid in the first type and withsodium tetraphenylborate solution in the seconde type . Direct method, standardadditions method and multi standard additions method have been alsosuccessfully applied and showing a very goodresults.The results of the normal spectra were compared withsulfamethoxazoleelectrodes results by using F-test statistics. The results of these analytical methods were showed to be simple, rapid and with good accuracy.

2- Experimental part

2-1-Instruments and equipment:-

1- A digital pH/ion meter (inoLab 740 with terminal 740 – WTW,Germany) as shown in figure (2 - 1).

Figure 2-1:- **A digital pH/ion meter (inoLab 740 with terminal 740 – WTW,**

2-Double-beam UV-Visible spectrophotometer model (UV-1650 PC) SHIMADZO (Japan), interfaced with computer via a SHIMADZU UV probe data system program (Version 1.10), using 1.00 cm quartz cells, (W. Germany)as shown in figure(2-2).

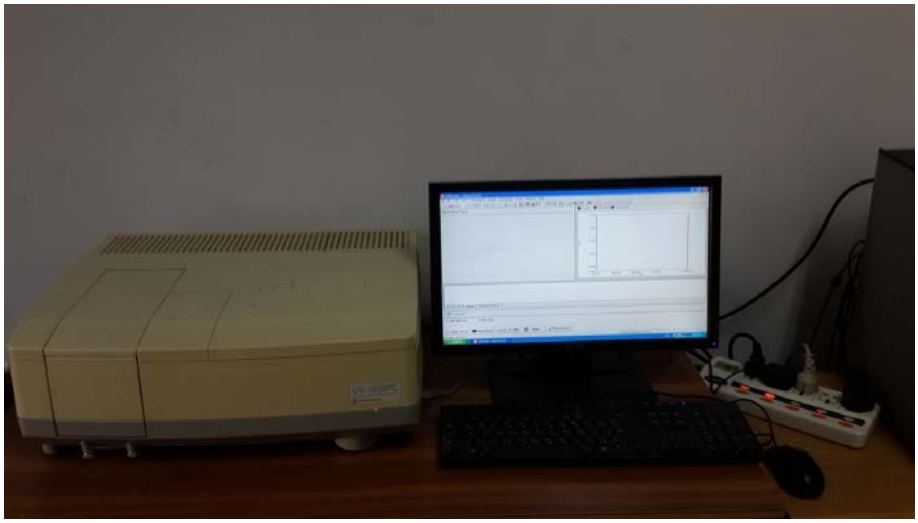


Figure 2-2:- **Double-beam UV-Visible spectrophotometer model (UV-1650 PC) SHIMADZO(Japan).**

3- Fourier transforms infrared spectrophotometer (FTIR-8300 SHIMADZU, Japan).

4- Reference electrode double junction, Orion, model 90-01.

5- pH combination glass electrode (SenTix® 82 WTW, Germany).

6- Silver-silver chloride wire.

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

8- Hotplate Magnetic stirrer (LMS-1003, DaihanLabtech).

9-Sartorius Handy 4 digits Analytical Balance (GMBH, H110, Germany).

10- Micropipettes (200-1000µl) and 25µl (Swiss made).

2-2-Chemicals:-

-Sulfamethoxazolestandard powder (purity 99%) was a gift from the State Company of Drug Industries andMedicalAppliances (Samara IRAQ-SDI).

-Trimole tabletseachTablet (containing 400 mgsulfamethoxazole (SMZ)) made by Julphar pharmaceutical limited company (U.A.E).

The chemical compounds were used throughout the study are listed in Table2-1.

Table 2-1: Shows types of used chemicals compounds.

Chemicals	Molecular formula	Formula Weight (g/mole)	Density g/mL at 25°C	Viscosity (CST)	Purity	Company
Poly vinyl chloride(PVC)	((CH2-CHCl)2)n	Breon S 110/10 B.P	---	---	99.5%	U. K. Ltd
Sodium tetra-phenyl borate (NaTPB)	$C_{24}H_{20}BNa$	342.22	---	---	98%	Fluka
Tungestophosphoric acid(TPA)	$H_3PW_{12}O_{40}$	2880.21	---	---	98%	Fluka
Hydrochloric acid	HCl	36.45	1.19	---	36%	Fluka
Sodiumhydroxide	NaOH	40.00	---	---	98%	BDH
Tetra-hydrofuran (THF)	C_4H_8O	72.11	0.889	---	99%	Fluka
Acetone	$(CH_3)_2CO$	58.08	0.791	---	99%	Fluka
Sulfamethoxazole(SMZ)	$C_{10}H_{11}N_3O_3S$	253.3	---	---	99%	SDI
Di-octylphthalate(DOP)	$C_6H_4[CO_2C_8H_{17}]_2$	390.56	0.985	82.98	99.5%	Fluka
Acetophenone (AP)	$CH_3CO(C_6H_5)$	120.15	1.03	1.62	98%	Fluka
Tri-butylphosphate (TBP)	$C_{12}H_{27}O_4P$	266.31	0.972	3.114	97%	Fluka
O-nitrophenyloctylether (ONPOE)	$O_2NC_6H_4OC_8H_{17}$	251.32	1.04	11.44	98%	Fluka
Tri-butylphthalate (TBPh)	$C_6H_4[CO_2CH_3(CH_2)_3]_3$	379.11	1.068	16.44	99%	Fluka
Nitrobenzene(NB)	$C_6H_5NO_2$	123.06	1.199	1.863	99%	Fluka
Trimethoprim	$C_{14}H_{18}N_4O_3$	290.32	---	---	99%	SDI
Potassiumchloride	KCl	74.55	---	---	98.5%	BDH
Sodium chloride -	NaCl	58.45	--	---	99%	BDH
Copper (II)sulfate anhydrous	$CuSO_4$	159.62	---	---	98%	Fluka
Manganese (II) sulfateanhydrous	$MnSO_4$	151	---	---	99%	Fluka
Ferric (III) sulfate	$Fe_2(SO_4)_3.9H_2O$	562	---	---	99%	BDH
Aluminum (III) chloride	$AlCl_3.6H_2O$	241.43	---	---	98.5%	Fluka
Starch	$(C_6H_{10}O_5)^n$	162.16	---	---	99%	BDH
Sucrose	$C_{12}H_{22}O_{11}$	342.30	---	---	99%	BDH

2-3-Preparation of standard solutions:-

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

1- 20% acetone solution was prepared by diluting 200mL of acetone and completing the solution up to 1000 mL with distilled water.

2- A stock solution of 10^{-2} M sulfamethoxazole (SMZ) was prepared by dissolving 0.1266 g of pure (SMZ) in10 mL acetone and completing the solution up to 50 mL volumetric flask with a solvent .The working solutions 10^{-8}-10^{-2} M SMZ were prepared by serial dilution of the stock solution using the same solvent.

3-The stock standard solution of 0.01M tugestophosphoric acid (TPA)was prepared by dissolving 1.4401g in distilled water and diluted up to 50mLby distilled water.

4-The stock standard solution of 0.01 M sodium tetraphenylborate (NaTPB) was prepared by dissolving 0.1711 g in 10mL acetone and diluted up to 50 mL with distilled water.

5- Stock solutions of 0.1 M ofNaCl, KCl, $CuSO_4$, $MnSO_4$, $Fe_2(SO_4)_3.9H_2O$, $AlCl_3.6H_2O$, sucrose, gelateinand trimethibrim were prepared by weighted (0.2922, 0.3727, 0.7981, 0.7550,2.81, 1.2071, 1.7115 and 1.50 g) and dissolved by distilled water in 50mL volumetric flask. More diluted solutions were prepared by dilutionfrom the stock solutions as required.

6-Diluted hydrochloric acid 0.1 M was prepared approximately by diluting 1 mL of 12 M HCl concentrated stoke solution to 100 mL by distilled water, and 0.1 M ofNaOH was prepared by weighting 0.4 g of NaOH and dissolving it in 100mL by distilled water.

2-4-Preparation of ion-pair compounds:-

1- The preparation ofion-pair of (SMZ-TPA) was prepared by mixing 50 mL of 0.01 M solution of sulfamethoxazole (SMZ) with 50 mL of 0.01 M tungestophosphoric acid (TPA)dissolved indistilled waterwith stirring. The resulting a white precipitate formedafter 24 hr, filtered, washed with water, dried at room temperature for two days using the vacuum desiccator..

2- The other ion-pair of (SMZ-NaTPB) was prepared by mixing 50 mL of 0.01 M solution of sulfamethoxazole (SMZ) with 50 mL of 0.01 M sodium tetra phenyl borate (TPA). The resulting precipitates were filtered off, washed with water, dried atroom temperature for two days using the vacuum desiccator.

Thecomposition of the two ion-pair compound (SMZ-TPA) and (SMZ-NaTPB) was confirmed using FTIR .

2-5-Preparation of sulfamethoxazoleelectrodes:-

2-5-1- Composition of membrane:-

-Foursulfamethoxazole ion-selective electrodes were prepared depending on the use of ion-pair compounds sulfamethoxazole-tungestophosphoricacid (SMZ-TPA)as the electro-active substance with fourplasticizers (E1, E2, E3, E4).

-Six sulfamethoxazole ion-selective electrodes were prepared based on the use of ion-pair compounds sulfamethoxazole-sodium tetra phenyl borate (SMZ-NaTPB) as the electro-active substance with sixplasticizers(L1, L2, L3, L4, L5, L6). The method of immobilization the ion-pair compounds into the PVC matrix membrane as described by Craggs et al[75]. 0.0400 g of electro-active precipitateswere mixed with 0.3600 g of plasticizer and 0.1700 g of PVC powder; all were dissolved in 5 mL of THF with stirring until a clear viscous solution was obtained[75].

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

Step1:The above solution poured into a glass casting ring about 30mm length and 35mm in diameter. It consists of two pieces; oneof them is the glass cylinder and the other is glass plate. The two pieces was pasted together by using (PVC-THF) viscous mixture (to make sure no loss in the membrane mixture).

Step 2:The top side of the cylinder was covered with a pad of filter paper on which a heavy weight was placed. The assembly was left for 2-3 days to allowgraduate evaporation of the solvent.

Step 3:The glass ring with adhering membrane was carefully removed from the glass plates .

Step 4: The membrane was then detached away from the edge of the ring. A disc of the membrane was cut equal to the external diameter of a PVC tube.

Step 5:One of sides of PVC tubing was flatted and smoothed by placing it on glass plate moisture with THF with aid of vertical rotation.The disc then mounted with a forceps on thepolished end, the outer edge of the disc membrane was carefully sealed to the end of the PVC tube.

Step 6:Next step is connection into a glass tube.

Step 7:The other side of the glass tube was assembled with plastic cover in which Ag/AgClwire was inserted through it, the tube was filled 3/4 with 0.001 M sulfamethoxazole solution before fixing the cover.

Step8:The electrode was then conditioned by placing it in 0.001M solution to be measured (at least 2 hour's) before using. Figure 2-3shows the Assembling the ion selective electrode.

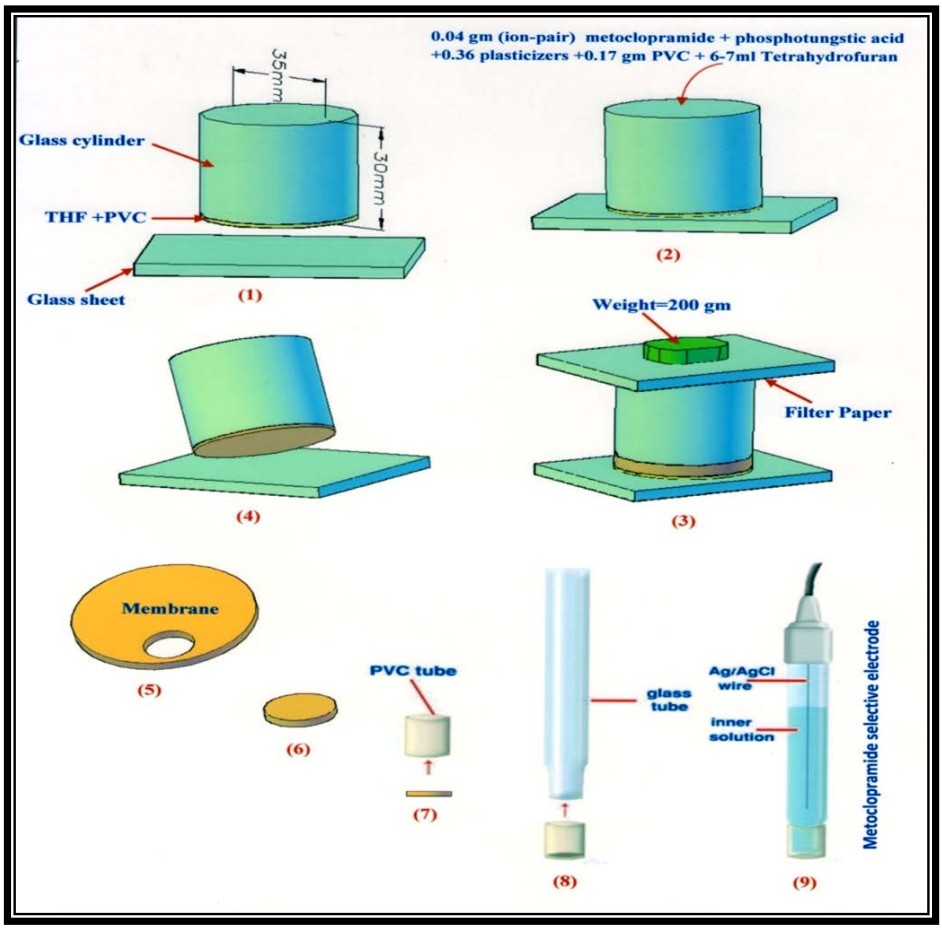


Figure 2-3:- Assembling the ionselective electrode. [75]

2-6-Potential measurement:-

The potentiometric cell was arranged by immersing the ion selective electrode and reference electrode inabeaker50 mLcontaining 25 mL of analyte standard solution. 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^{-2}-10^{-8} M). The calibration curves were prepared by plotting the potential (E) versus the logarithm of analyteconcentration by using a computer program (Microsoft office Excel 2010). From the calibration curve, characterization parametersof an

ISE were obtained, including; concentration range; slope and detection limit.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.

2-7-Effect of pH:-

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 1 to 11; obtained by addition few drops of hydrochloric acid and/or sodium hydroxide solutions.

2-8-Selectivity measurements:-

The effect of some species (Na^{+}, K^{+}, Mn^{2+}, Cu^{2+}, Fe^{3+}, Al^{3+}, starch, trimethoprim,sucrose andgelatein). For the ion selective electrodes the selectivity coefficients were determined by[52]:

2-8-1-The separate solution methods[53,54]:-

In this method, a 25 mL of $1x10^{-3}$ M solution of the prepared analyte (A) (sulfamethoxazole) and 25 mL of $1x10^{-3}$ M of each other interfering ion (B) (Na^{+}, K^{+}, Mn^{2+}, Cu^{2+}, Fe^{3+}, Al^{3+}, trimethoprim, starch, sucrose and gelatin) for sulfamethoxazole electrodes. The potential of each solution is measured separately. The selectivity coefficient was calculated according to equation 1-8.

2-8-2-Mixed solution methods[fixed interference method(FIM)][55,56]:-

In this method, a 10 mL of analyte(A) solution (sulfamethoxazole) in concentration range10^{-8} to 10^{-2} M was mixed with 10mL of 0.1M 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 1-8. The values of selectivity coefficient ($K^{pot}_{A,B}$) are calculated according to equation 1-9. The activities of interfering ion (a_B) are calculated after dilution:-

$a_B = (0.1M \times 10mL)/ 20mL = 5\times10^{-2}$ M……2-1

howeverthere is some differences in the vales of interferences between separate and mixed method[76].

2-9-Sample analyses:-

2-9-1-Direct method [62]:-

The potentiometric measurementsoftheanalyte (A) solution (sulfamethoxazole) indicator electrodes. The concentration was then calculated using the calibration curve for the standard analyte (A).

2-9-2-Standard additions method (SAM)[62, 63]:-

In this method, the sample of 25mL with concentration of $1x10^{-4}$M is introduced in to the potentiometric cell followedby addition of 0.5 mL of 0.01 M increment of analyte (A) solution (sulfamethoxazole). The potential was measured before and afteraddition[77]. In this method, the sample of 25 mL with concentration of $1x10^{-4}$M is introduced followedby addition of 0.5 mL of 0.001 M increment of analyte (A) solution (sulfamethoxazole). The potential were measured before and after addition[78].

2-9-3-Multiple standard additions method[64]:-

This method is an extension of standard additionsmethod; the sample of 25 mL of $1x10^{-4}$M is introduced in to the potentiometric cell followed by addition of 0.5 mL of 0.001 M of analyte (A) solution (sulfamethoxazole). The potential is recorded before and after each addition.

2-9-4-Potentiometric titration method[65]:-

2-9-4-1-Sulfamethoxazole electrodes:-

A precipitation titration was performed for the sulfamethoxazole sample under study. In this method, 15 mL sample solution containing sulfamethoxazole1×10^{-4}M was titrated against 1×10^{-4}M tungestophosphoric acid(TPA) 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 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 in first derivativesandto calculate thechange(change in potential) per unit volume of titrantΔ ($\Delta E/\Delta V$) plotted versus the average volume of titrant, the point in the middle between the two peak is the end point in second derivaties.

2-10-Preparation of pharmaceutical formulation:-

Ten tablets of trimole each tablet containing 400 mg of sulfamethoxazoleweighted accurately and grinded it found that the weight of average of one tablet was 0.6656 g. To prepare 10^{-2} M from sulfamethoxazole 0.2107g wasdissolved in 10 mL acetone and then filtered and completing the solution up to 50 mLother samples prepared by dilution using the solvent of(20% acetone with 80% distilled water).

2-11-Spectrophotometric Studies[72,73]*:-*

2-11-1-Standard solution for sulfamethoxazole:-

- 20% acetone solution was prepared by diluting 200mL of acetone and completing the solution up to 1000 mL with distilled water.

-A series of solutions ($0.990x10^{-4}$, $0.996x10^{-4}$, $0.999x10^{-4}$, $1.004x10^{-4}$, $1.005x10^{-4}$)Mwere preparedfrom ($1x10^{-3}$)Msulfamethoxazoleby using the above solution .

2-11-2-FTIR absorption spectra for puresulfamethoxazoleandsulfamethoxazolecomplexes(SMZ-TPA) sulfamethoxazole with tungestophosphoric acid andsulfamethoxazole with sodium tetraphenyl borate(SMZ-NaTPB)complex:-

A small amount of SMZ and the complex (SMZ-TPA) and (SMZ-NaTPB)samples were driedto 70 ^{0}C for nearly one hour andFTIR spectra in the range (4000-400) cm^{-1}were recorded using potassium bromide disk.The samples were confirmed using FTIR instrument.

3-Results and Discussion

3-1-(Sulfamethoxazole-Tungestophosphoric acid) electrodes:-

3-1-1- FTIR spectrum of pure sulfamethoxazole and complex (sulfamethoxazole –tungestophosphoric acid):-

The FTIR spectrum of the complex was compared with the reference spectrum of sulfamethoxazole , Fig.(3- a and b). the functional groups obtained from the spectrum were shown in table (3-1) . The value of N-H bond change from 3463 to 3199 that is mean the mono bond between SMZ and TPA and some bonds still the same with little changes.

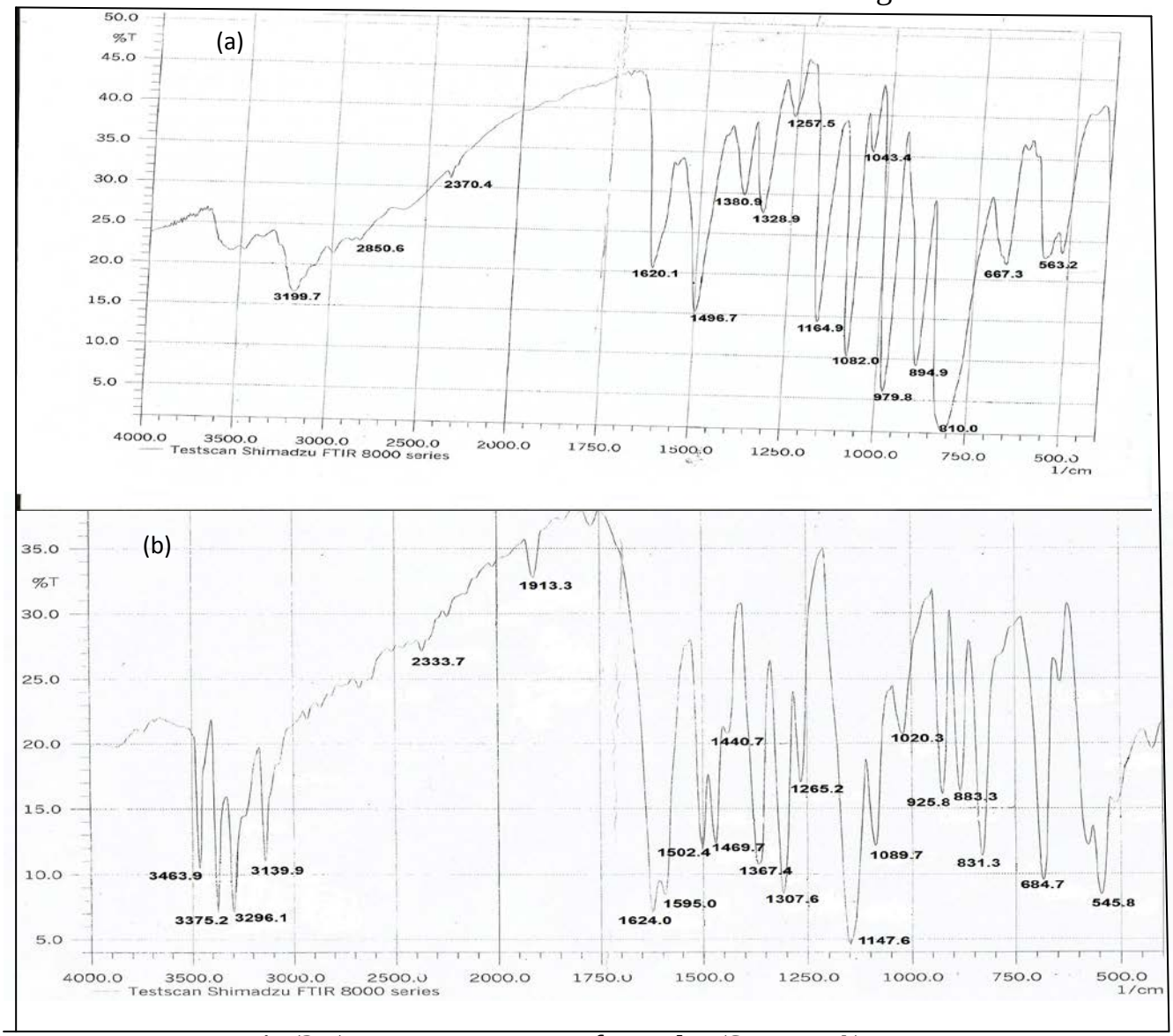


Fig.(3-1) a- FTIR spectrum of complex (SMZ-TPA).
b- FTIR reference spectrum of pure SMZ.

Table (3-1):-The functional groups obtained from the spectrum for each SMZ and complex [SMZ-TPA].

Functional groups	Sulfamethoxazole(SMZ) cm^{-1}	Complex [SMZ-TPA] cm^{-1}
ν (N-H)	3463	3199
ν (S=O)	1367	1380
ν (N=C)	1624	1620
ν (N-O)	1502	1496

3-1-2- Characteristics of (E1, E2, E3 and E4) electrodes :-

E1, E2, E3and E4 were four ion selective electrodes based on using sulfamethoxazole (SMZ) and tungestophosphoric acid (TPA) using four plasticizers; Di- octyl phthalate (DOPH); Tri-butyl phosphate (TBP); Acetophenone (AP) and Nitrobenzene (NB) in PVC matrix were examined. Sulfamethoxazole selective electrodes (E1, E2, E3 and E4) which their calibration curves shown in Figure 3-2(a, b, c and d) respectively. The effects of different plasticizers were studied with respect to the linear range of concentration, detection limit, slope, response time and lifetime of the measured electrode as in table (3-2). The electrode with good characteristics was used for further studies.

These electrodes gave linear range from ($1x10^{-5}$-$1x10^{-2}$ M, $1x10^{-7}$-$1x10^{-2}$ M, $1x10^{-5}$-$1x10^{-2}$ M and $1x10^{-5}$-$1x10^{-2}$ M) and gave the slopes of (52.008, 58.381, 56.909 and 50.309 mV/decade), with detection limit (9×10^{-6}M, 1×10^{-8} M, $6\times10^{-6}$and 7×10^{-6}M) respectively. E2 electrode is the best electrode that gave the Nernst slope of 58.381mV/decade, with liner range $1x10^{-7}$–$1x10^{-2}$ M. This may be due to the compatibility between the components of the membrane .

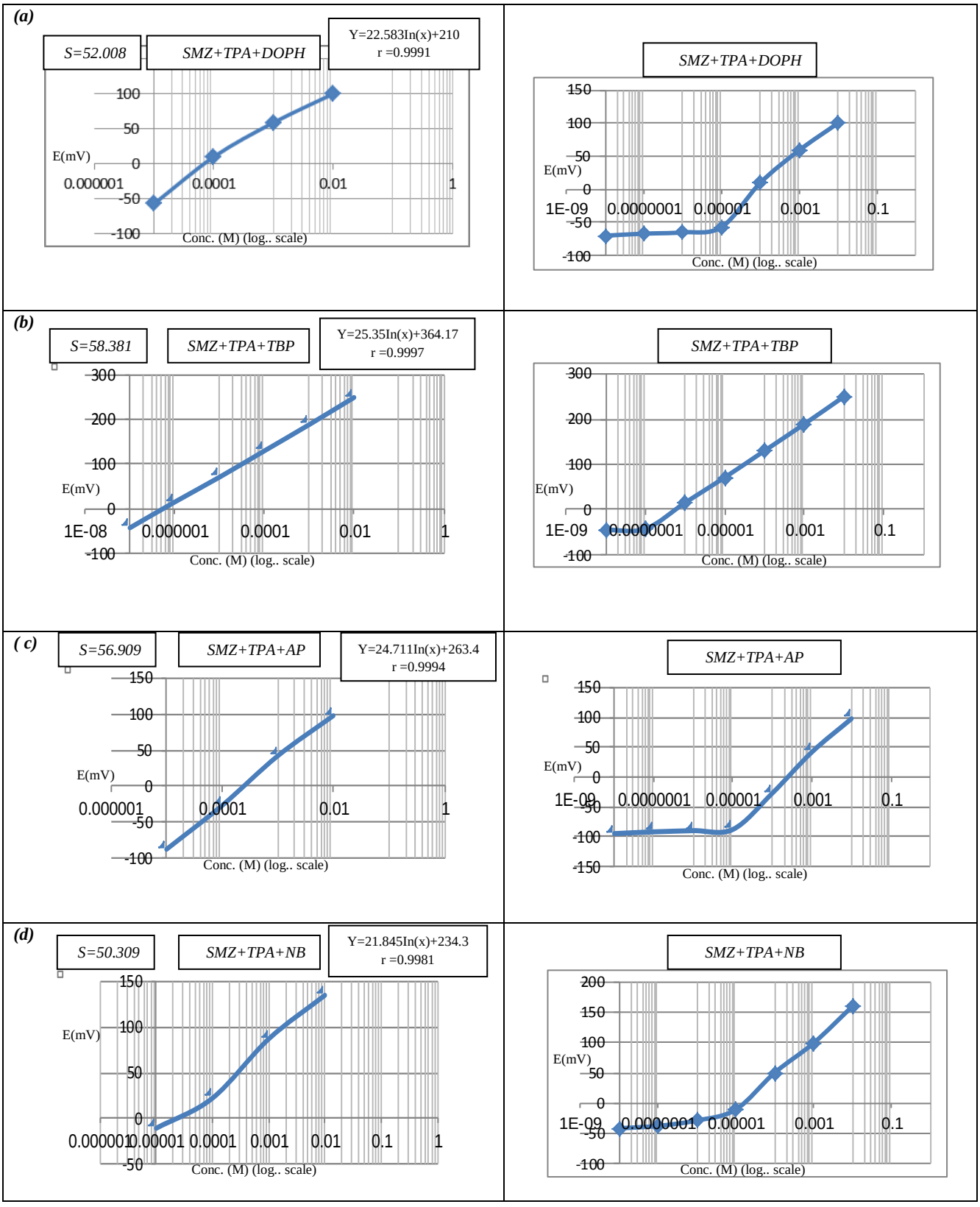


Figure 3-2:-The calibration curves of sulfamethoxazole electrodes used different plasticizers: a-E1 electrode, b-E2 electrode, c-E3 electrode, d-E4 electrode

E2 electrode, gave a slope of 58.381 mV/decade. This Nernest slope may be due to the ion exchange between components of the complex and due to the viscosity of TBP plasticizer (3.114 cst). But the other membranes (SMZ+ONPOE) and (SMZ+TBPH) became solid as shown in fig. (3-3) (a ana b) . This could be due to the ion exchange there is no ion exchange between components of the complex .

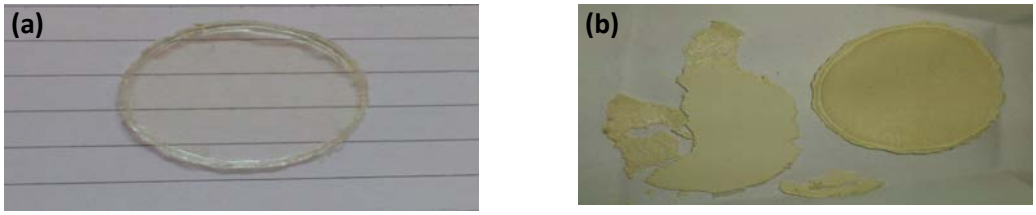


Figure (3-3) (a) figure of best electrode (SMZ- TPA-TBP). (b) figure of worst electrode (SMZ- TPA-ONPOE).

This Nernest slope for E2 electrode was observed during the long time period of 27 days. Then after 27 days, the electrode characteristics drifted away from the Nernst behavior.

Table 3-2:- The equation of calibration curves, slope, correlation coefficient, linear range, detection limit, response time and lifetime for sulfamethoxazole electrodes.

Electrode	Linear equation	Correlation coefficient (r)	Slope mV/Decade	Linear range (M)	Detection limit (M)	Response time (sec)			Life time (day)
						10^{-2}(M)	10^{-3}(M)	10^{-4} (M)	
E1 SMZ + TPA +DOPH	y = 22.583 Ln(x) + 210	0.9991	52.008	1×10^{-2}– 1×10^{-5}	9×10^{-6}	26	30	37	29
E2 SMZ + TPA +TBP	y = 25.35 Ln(x) + 364.17	0.9997	58.381	1×10^{-2}– 1×10^{-7}	9×10^{-8}	24	28	36	27
E3 SMZ + TPA +AP	y = 24.711 Ln(x) + 263.4	0.9994	56.909	1×10^{-2}– 1×10^{-5}	6×10^{-6}	29	36	42	20
E4 SMZ + TPA +NB	y = 21.845 Ln(x) + 234.3	0.9981	50.309	1×10^{-2}– 1×10^{-5}	7×10^{-6}	22	25	33	9

3-1-3-Effect of pH using E2 electrode:-

Three different concentrations (1×10^{-2}, $1\times10^{-3}$and 1×10^{-4}) M were used to examine the effect of pH on the electrode potentials for SMZ selective electrode (E2) by measuring the potential of the cell in SMZ solutions in which the pH ranged from (0.5-11.0). The results shown in Fig.(3-4). The pH adjusted by adding few drops of approximately (0.1) M of hydrochloric acid and/or sodium hydroxide solution. At pH values less than 1.6 or in very high acidity, the electrode response has been increased rather irregularly, this may be due to that the electrode start to response to H_+ activities as well as SMZ ions, and in an alkaline solution (pH greater than 7) the electrode response has been decreased, this may be due to the formation of complexes of SMZ . The working pH were tabulated in Table (3-3).

Table 3-3:- Working pH ranges for E2 electrode.

Electrode no.	*Composition of electrode E2*	*pH range*		
		1×10^{-2} (M)	*1×10^{-3} (M)*	*1×10^{-4} (M)*
E2	**SMZ+TPA+TBP**	**1.6-6.8**	**1.6-6.5**	**2.0-6.5**

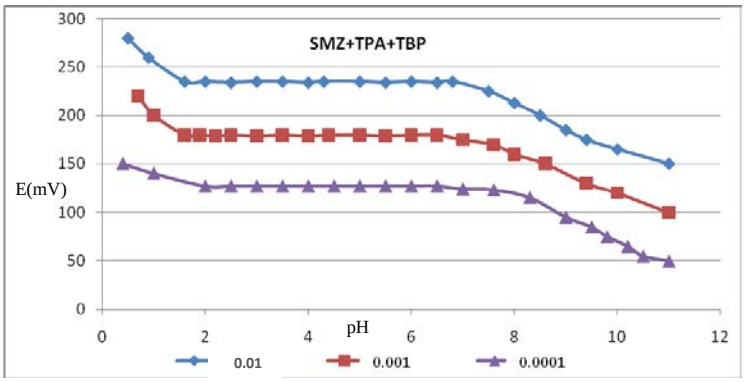


Figure 3-4: Effect of pH on the potential of the electrode E2 at concentrations 1×10^{-2}, 1×10^{-3} and 1×10^{-4}M.

3-1-4-Selectivity methods using E2 electrode:-

3-1-4-1-Separate solution methods using E2 electrode:-

25 mL of (a_A = a_B =10^{-3} M) The potential are measured with two separate solutions, measured values of E_A and E_B, respectively, the value of $K^{pot}_{A,B}$ is calculated by the equation 1-8. The results of selectivity coefficients are summarized in Table 3-4.

$$\log K^{pot}_{A,B}=(E_B-E_A)/S+(1-z_A/z_B)\log a_A \ldots\ldots..(1\text{-}8)$$

Where E_A, E_B; z_A, z_B; and a_A, are the potentials, charge numbers, and activities for the primary A ion, respectively, at a_A = a_B.The values of $K^{pot}_{A,B}$ for monovalent species is more than other species this could be due to monovalent species have same charge

Table 3-4:- Selectivity coefficient values for E2 electrode, when E_A=180mV and the slope 58.381mV/decade.

Interfering species	E_b	$\log K^{pot}_{A,B}$	$K^{pot}_{A,B}$
Na^+	57	-2.119	7.59×10^{-3}
K^+	52	-2.205	6.23×10^{-3}
Cu^{2+}	29	-4.102	7.91×10^{-5}
Mn^{2+}	21	-4.239	5.76×10^{-5}
Fe^{3+}	16	-4.825	1.49×10^{-5}
Al^{3+}	12	-4.894	1.27×10^{-5}
Trimethoprim	50	-2.239	5.75×10^{-3}
Starch	37	-2.464	3.43×10^{-3}
Sucrose	25	-2.670	2.13×10^{-3}
Gelatin	23	-2.705	1.97×10^{-3}

3-1-4-2-mixed methods(Fixed Interference Method)(FIM) using E2 electrode:-

The potential E (mV) values obtained are plotted vs. the logarithm of the activity of the sulfamethoxazole ion (a_A) with constant activity of interfering ion (a_B =0.1 M). The intersection of the extrapolated linear portions of this plot indicates the value of (a_A) from Figure 3-5 to Figure 3-14 can be used to calculate $K^{pot}_{A,B}$ from equation 1-9. all results of $K^{pot}_{A,B}$ were shown in Table 3-5.

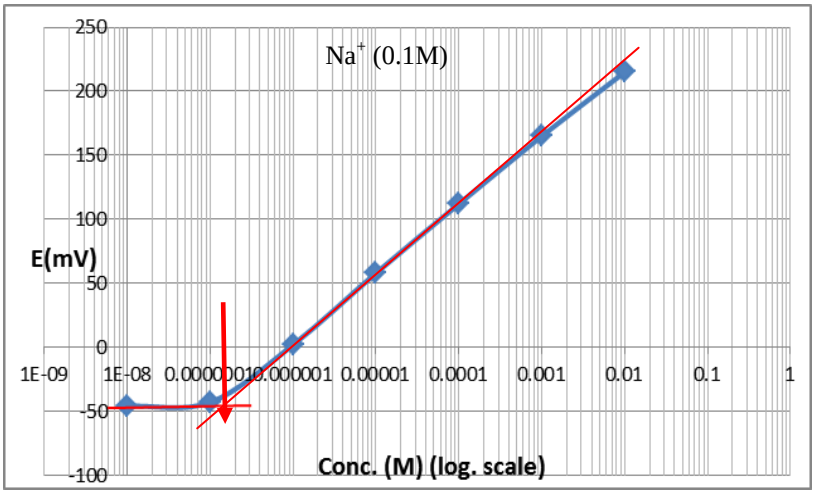


Figure 3-5:- FIM calibration curve for E2 electrode, Na^+ (5×10^{-2}M) as interfering ion $a_A=1.7\times10^{-7}$M.

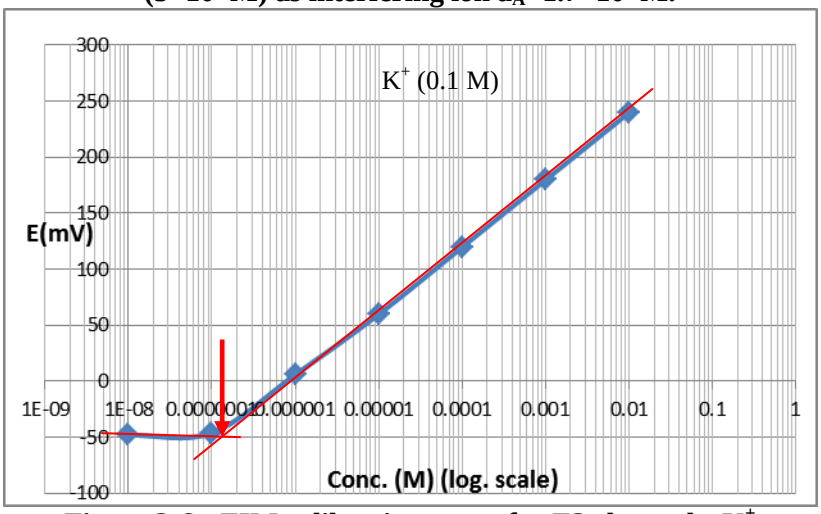


Figure 3-6:- FIM calibration curve for E2 electrode, K^+ (5×10^{-2}M) as interfering ion $a_A=1.5\times10^{-7}$M.

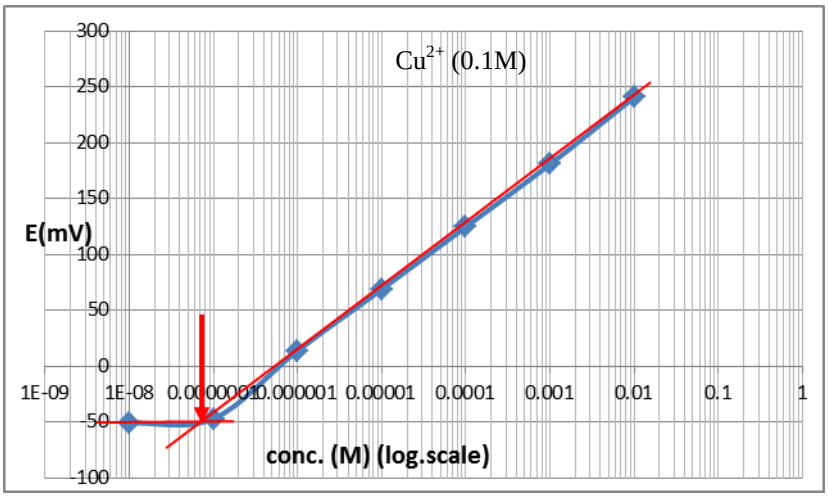


Figure 3-7:- FIM calibration curve for E2 electrode, Cu^{2+} (5×10^{-2}M) as interfering ion $a_A=7.5\times10^{-8}$M.

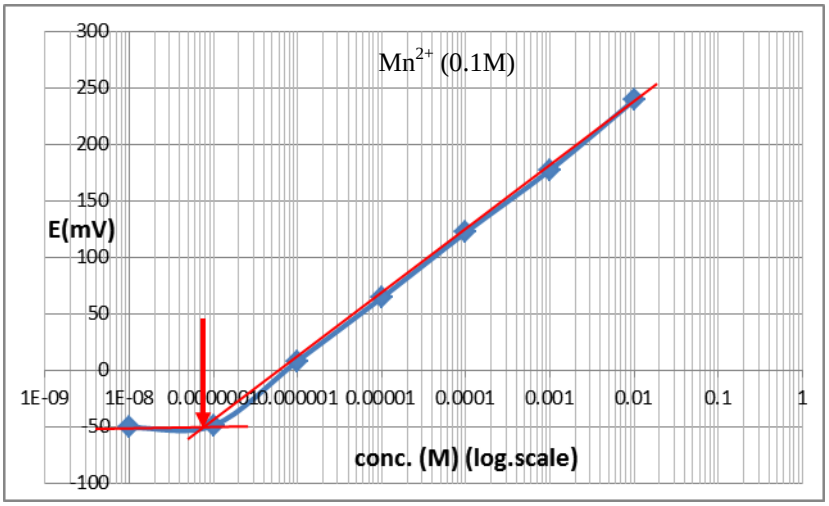


Figure 3-8:- FIM calibration curve for E2 electrode, Mn^{2+} (5×10^{-2}M) as interfering ion $a_A=8\times10^{-8}$M.

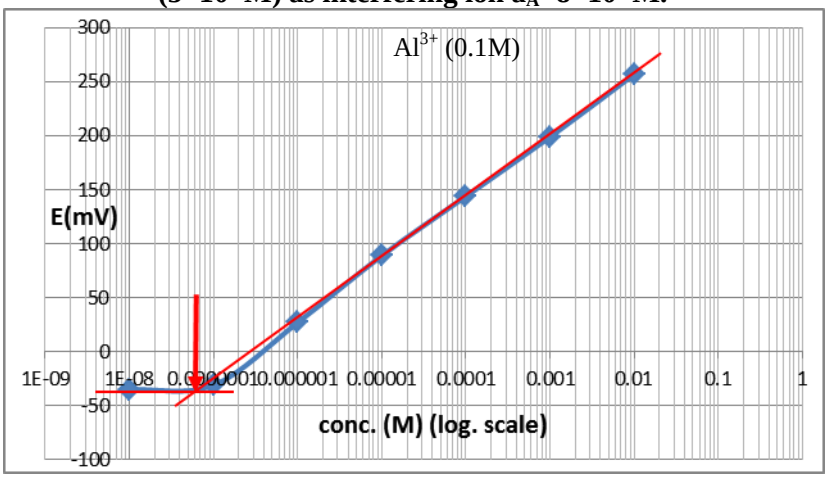


Figure 3-9:- FIM calibration curve for E2 electrode, Al^{3+} (5×10^{-2}M) as interfering ion $a_A=6\times10^{-8}$M.

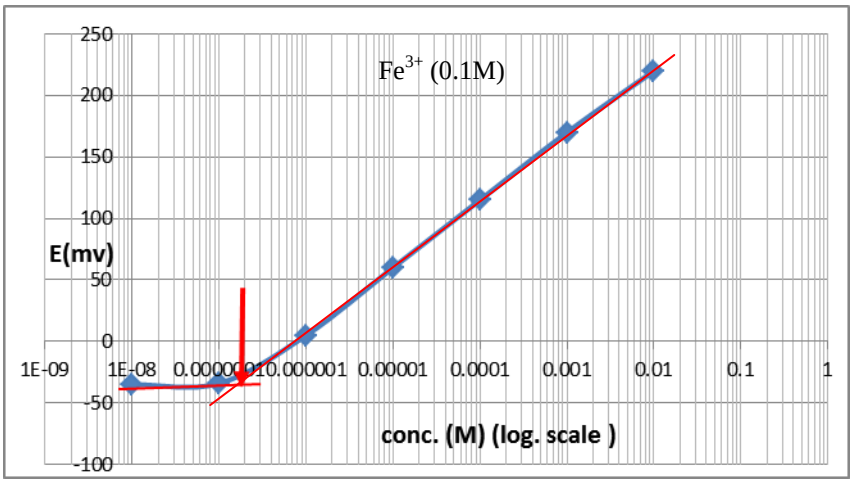


Figure 3-10:- FIM calibration curve for E2 electrode, Fe^{3+} (5×10^{-2}M) as interfering ion $a_A=2\times10^{-7}$M.

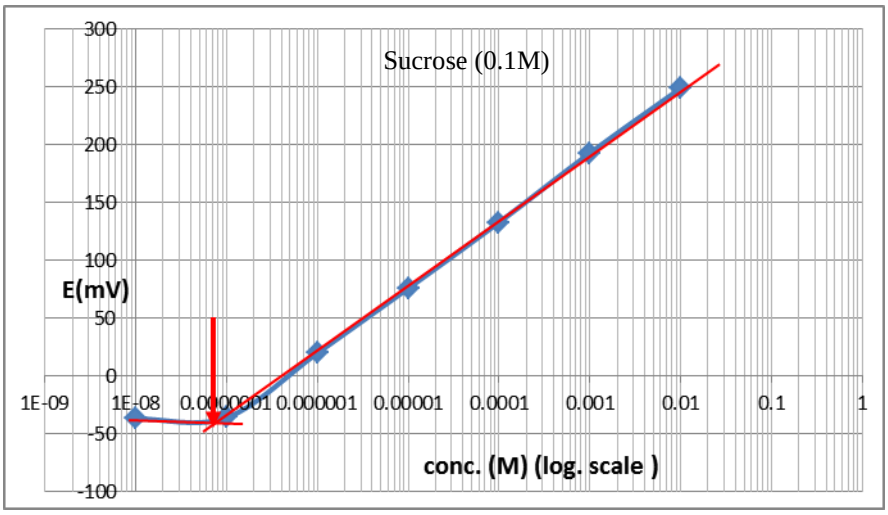


Figure 3-11:- FIM calibration curve for E2 electrode, sucrose (5×10^{-2}M) as interfering ion $a_A=7\times10^{-8}$M.

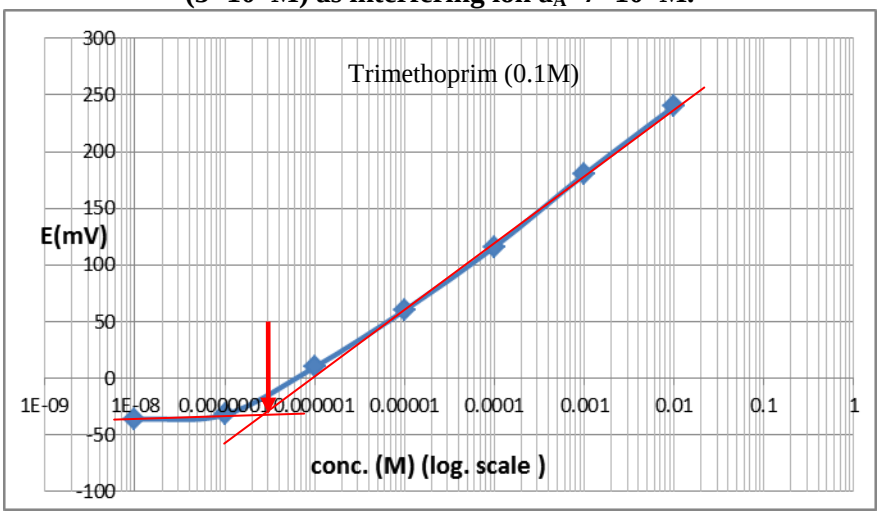


Figure 3-12:- FIM calibration curve for E2 electrode, trimethoprim (5×10^{-2}M) as interfering ion $a_A=3\times10^{-7}$M.

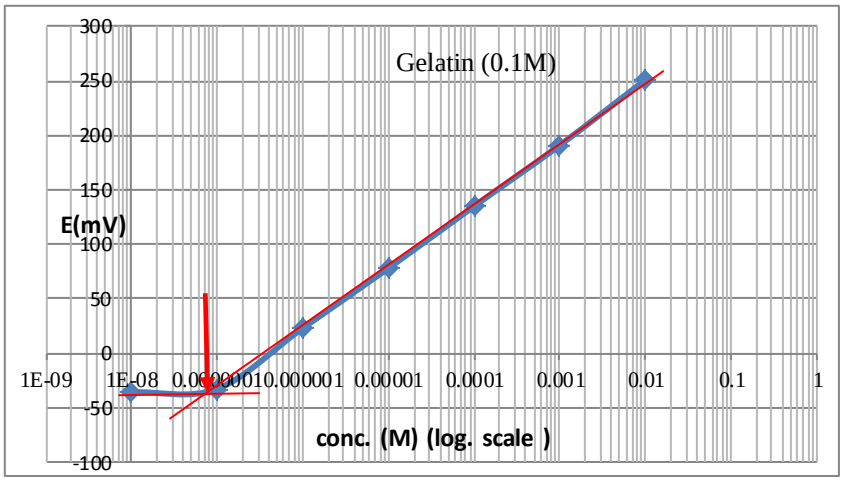


Figure 3-13:- FIM calibration curve for E2 electrode, gelatine (5×10^{-2}M) as interfering ion $a_A=6.5\times10^{-8}$M.

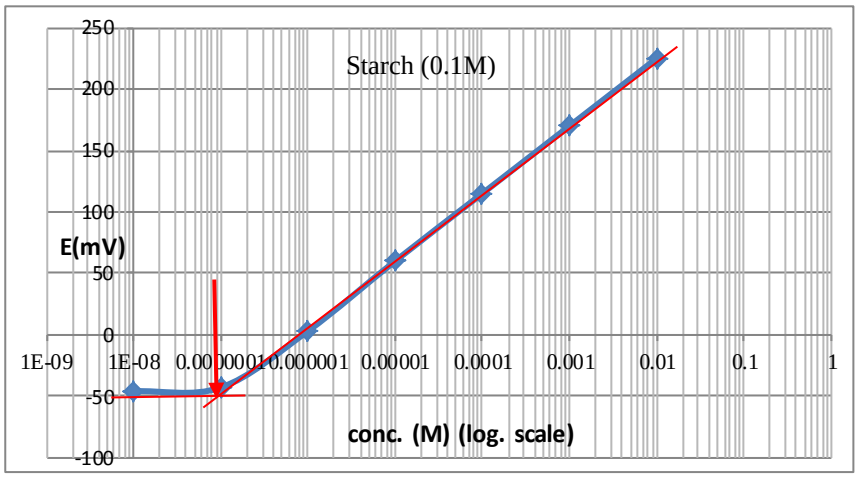


Figure 3-14:- FIM calibration curve for E2 electrode, starch (5×10^{-2}M) as interfering ion $a_A=9\times10^{-8}$M.

Table 3-5:- Values of $K^{pot}_{A,B}$ according to FIM, when $a_B = 5x10^{-2}$ M.

	$a_b = 5\times10^{-2}$	
Interfering ions	a_a	$K^{pot}_{A,B}$
Na^+	1.7×10^{-7}	3.40×10^{-6}
K^+	1.5×10^{-7}	3.00×10^{-6}
Cu^{2+}	7.5×10^{-8}	3.35×10^{-7}
Mn^{2+}	8.0×10^{-8}	3.57×10^{-7}
Fe^{3+}	2.0×10^{-7}	5.42×10^{-7}
Al^{3+}	6.0×10^{-8}	1.62×10^{-7}
Trimethoprim	3.0×10^{-7}	6.00×10^{-6}
Starch	9.0×10^{-8}	1.80×10^{-6}
Sucrose	7.0×10^{-8}	1.40×10^{-6}
Gelatin	6.5×10^{-8}	1.30×10^{-6}

3-1-5- Sample analyses using E2 electrode:-

3-1-5-1- Direct method 0f E2 electrode:

The calibration curve was constructed for E2 electrode, as shown in Fig.3-15, and the concentration of the unknown was calculated from the linear equation y=25.35Ln(x) + 364.17 of the calibration curve which has the slope S =58.381 mV/decade and the intercept = 364.17, for n=5, the results are listed in table 3-6.

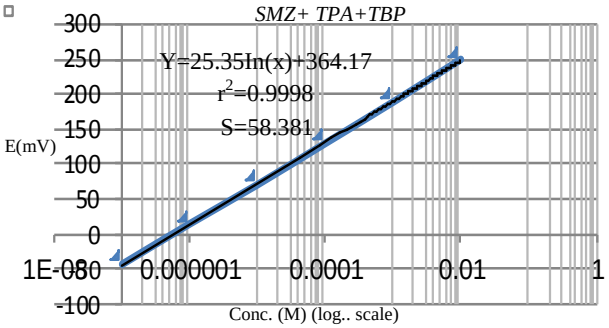


figure 3-15:- Calibration curve of E2 electrode.

Table 3-6:- Calculation for five samples of sulfamethoxazole standard solution 10^{-4} M using direct method for E2 electrode, where slope = 58.381 mV/decade.

Potential reading E(mV)	The conc. of SMZ solution calculated from linear equation/(M)	*δn-1**	$\overline{X} \pm (ts/\sqrt{N})$	Re %	E_r%	RSD%
130.51	0.993×10^{-4}	4.098×10^{-7}	$0.996 \times 10^{-4} \pm 0.494 \times 10^{-6}$	99.3%	-0.7%	0.411%
130.65	0.998×10^{-4}			99.8%	-0.2%	
130.49	0.992×10^{-4}			99.2%	-0.8%	
130.74	1.002×10^{-4}			100.2%	0.2%	
130.66	0.998×10^{-4}			99.8 %	-0.2%	

δn-1:standard deviation, t=2.78 for N=5.*

3-1-5-2-Standard additions method (SAM) of E2 electrode:

It has been carried out by a procedure that 0.5 mL increment of 10^{-3} M sulfamethoxazole as standard was added to 25 mL of sample as unknown [71]. The results of calculation (SAM) for the sulfamethoxazole solution using (E2) electrode. and equation 1-12, recovery, relative error and relative standard deviation for five additions of sulfamethoxazole are listed in Table 3-7.

Table 3-7:- Calculation for five additions of sulfamethoxazole standard solution using (SAM) for E2 electrode, where slope=58.381mV/decade, at concentration of sample 10^{-4} M.

V_S (mL) added	E (mV)	ΔE	(V_U/V_S)	Antilog (ΔE/S)	C_U/(M)	*δn-1**	$\bar{X}\pm(ts/\sqrt{N})$	Re%	E_r%	RSD%
0	130	--------	∞	1	----------	5.029×10^{-7}	$0.987\times10^{-4}\pm0.607\times10^{-6}$	----------	----------	0.509%
0.5	135.11	5.11	50	1.2232	0.986×10^{-4}			98.60%	-1.4%	
1.0	138.42	8.42	25	1.3938	0.996×10^{-4}			99.60%	-0.4%	
1.5	141.55	11.55	16.66	1.5770	0.983×10^{-4}			98.30%	-1.7%	
2.0	145.23	15.23	12.5	1.8234	0.985×10^{-4}			98.50%	-1.5%	
2.5	147.48	17.48	10	1.9926	0.988×10^{-4}			98.80%	-1.2%	

δn-1*:standard deviation, t=2.78 for N=5.

3-1-5-3- Multi standard additions method (MSA)of E2 electrode:

The calibration curve for MSA for (E2) electrode was shown in Figure (3-16) by plotting antilog (E/S) versus the volume of the five different additions of standard sulfamethoxazole . From

the equation of the calibration curve the volume (mL) at intercept with X axis for the curve was calculate, the concentration of the unknow sample (C_U) was calculated using the equation 1-15. The volume at intercept with X axis, concentration of the unknown sample (C_U), the analysis results %Re and %Er are listed in Table 3-8.

Vol.(mL) of std. add	E(mV)	Antilog (E/S)
0	130	168.559
0.5	135.11	206.196
1	138.42	234.951
1.5	141.55	265.822
2	145.23	307.344
2.5	147.48	335.865

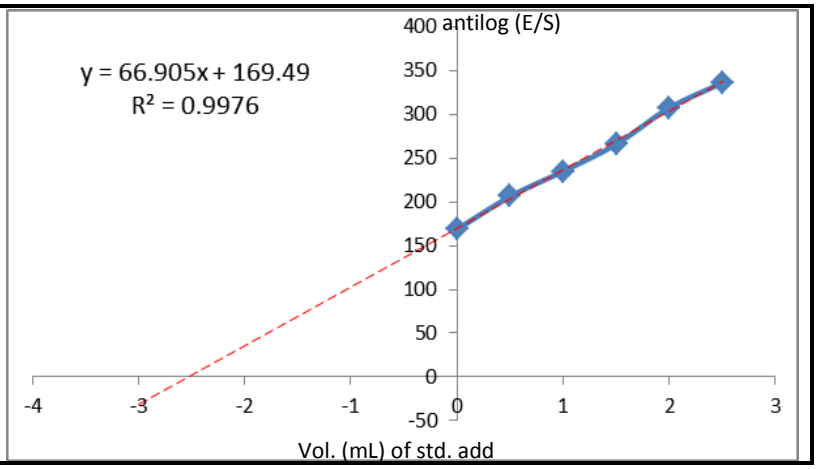
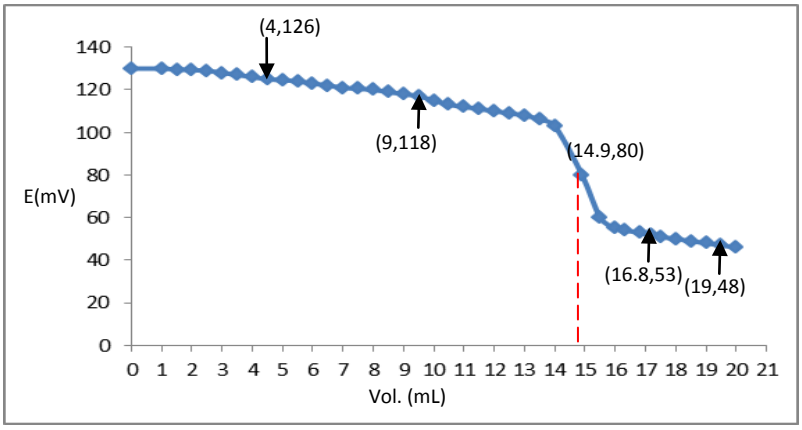


Figure 3-16:- Calibration curve of antilog (E/S) versus the volume added of standard 10^{-3}M for determination of 25 mL sulfamethoxazole solution 10^{-4}M by (MSA).

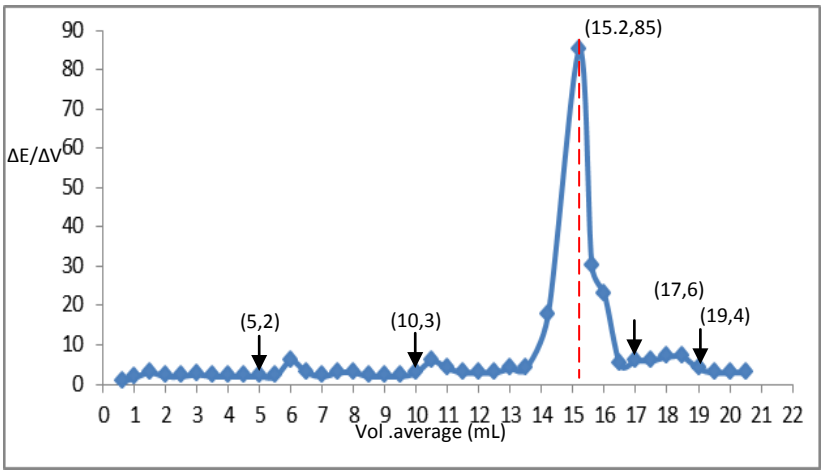
Table 3-8:- The linear equation of the calibration, correlation coefficient, volume at intercept, the concentration of sample (C_U), E_r% and Re% of the unknown sample.

Linear equation	*r*	Volume at intercept (mL)	C_U(M)	Re%	E_r%
Y=66.905x+169.49	0.9987	2.533	1.013×10^{-4}	101.320%	1.320%

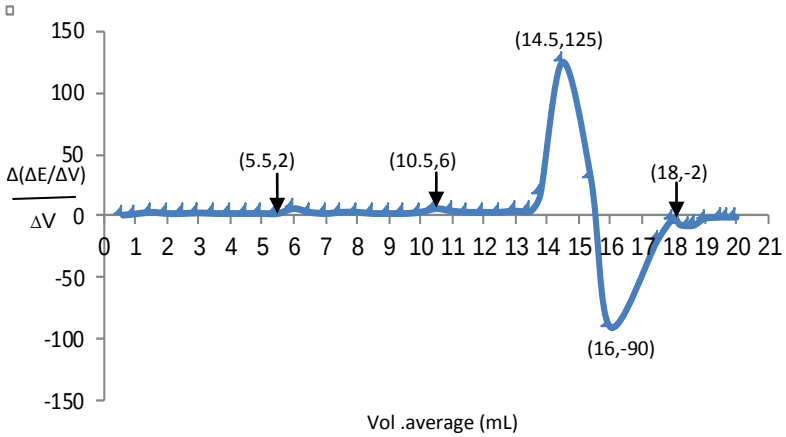
3-1-5-4-Titration method of E2 electrode: The potentiometric titration for 15 mL of 10^{-4} M of sulfamethoxazole solution with 10^{-4} M of tungestophosphoric acid as titrant solution as shown in Figure 3-17(a, b, c) , the results of titration (Re%, E_r% and RSD%) are listed in Table 3-9.



(a) Titration curve



(b) Titration curve by using first derivative.



(c)Titration curve by using second derivative.

Figure 3-17 (a, b and c) Titration curve of E2, 15 mL sample solution 1×10-4 M sulfamethoxazole with 1×10-4M of (TPA) as a titrant solution.

Table 3-9:- Standard sulfamethoxazole solution analyses results by using titration method for E2 electrode.

Titration Figure(3-17)	Vol. mL at the end point	C_U(M)	Re%	RSD*%
Figure (a)	14.9	0.993×10^{-4}	99.333 %	1.659%
Figure (b)	15.2	1.013×10^{-4}	101.333%	
Figure (c)	15.4	1.026×10^{-4}	102.666	

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

the data obtained for E2 electrode using direct method, standard addition method, multi standard addition method and titration method were listed in Table 3-10.

Table 3-10:- Analysis of SMZ by potentiometric techniques by using ISE E2.

Parameter	Direct method*	SAM*	Multi SAM*	Titration method**
Conc.(M)	1.000×10^{-4}	1.000×10^{-4}	1.000×10^{-4}	1.000×10^{-4}
Found(M)	0.996×10^{-4}	0.987×10^{-4}	1.013×10^{-4}	1.011×10^{-4}
RSD*%	0.411%	0.509%	---------	1.659%
Re%	99.660%	98.760%	101.320%	101.110%
Er%	-0.340%	-1.24%	1.320%	1.110%
δn-1	4.098×10^{-7}	5.029×10^{-7}	---------	1.677×10^{-6}
$\bar{x} \pm (ts/\sqrt{N})$	$0.996\times10^{-4}\pm0.494\times10^{-6}$	$0.987\times10^{-4}\pm0.607\times10^{-6}$	---------	$1.011\times10^{-4}\pm0.416\times10^{-5}$

RSD**% for n=3, t=4.3.
RSD*% for n=5, t=2.7.

3-1-6-Analytical application of the selected electrode (E2) with drug:-

Due to the importance of the pharmaceutical products, in recent years, potentiometric measurement using ion-selective electrodes has found use in pharmaceuticals analyses. The (E2) electrode was proved to be useful in the potentiometric determination of sulfamethoxazole in pharmaceutical preparations.

3-1-6-1-Direct method for drug:-

The calibration curve was constructed and the concentration of the unknown was calculated from the linear equation y= 25.35 Ln(x) +364.17 of the calibration curve, and the results are listed in Table 3-11.

Table 3-11:- The results for five samples of standard solution at 10^{-4}M, using direct method for E2 electrode.

E(mV) for the sample	The conc. of sample calculated(M)	δ_{n-1}*	$\overline{X} \pm (ts/\sqrt{N})$	Re%	E_r%	RSD%
130.92	1.009×10^{-4}	6.457×10^{-7}	$0.998\times10^{-4}\pm 0.779\times10^{-6}$	100.9%	0.9%	0.646%
130.64	0.998×10^{-4}			99.8%	-0.2%	
130.56	0.995×10^{-4}			99.5%	-0.5%	
130.48	0.992×10^{-4}			99.2%	-0.8%	
130.60	0.997×10^{-4}			99.7%	-0.3%	

δn-1*: at t=2.78 for N=5.

3-1-6-2-standard additions method for drug:-

It carried out by a procedure that 0.5 mL increment of 10^{-3} M sulfamethoxazole as standard was added to 25 mL of sample as unknown. The results of calculation (SAM) by using (E2) electrode and equation 1-13, recovery, relative error and relative standard deviation for five additions of sulfamethoxazole are listed in Table 3-12.

Table 3-12:- The results for five additions of standard solution at concentration 10^{-3}M, for E2 electrode, where slope=58.381mV/decade.

V_S(mL) added	E(mV)	ΔE	(V_U/V_S)	Antilog (ΔE/S)	C_U/(M)	δ_{n-1}*	$\bar{X} \pm$ (ts/√N)	Re%	E_r %	RSD%
0	130	--------	∞	----------	--------	8.820×10^{-7}	$0.996\times10^{-4}\pm0.106\times10^{-5}$	--------	-------	0.885%
0.5	134.97	4.97	50	1.2165	0.989×10^{-4}			98.9%	-1.1%	
1.0	138.69	8.69	25	1.4088	0.999×10^{-4}			99.9%	-0.1%	
1.5	142.37	12.37	16.66	1.6288	0.998×10^{-4}			99.8%	-0.2%	
2.0	144.92	14.92	12.5	1.8012	1.009×10^{-4}			100.9%	0.9%	
2.5	147.75	17.75	10	2.0139	0.987×10^{-4}			98.7%	-1.3%	

δn-1* at t=2.78; N=5.

3-1-6-3-Multi standard additions method (MSA) for drug:-

The calibration curve for MSA for (E2) electrode was shown in Figure 3-18 by plotting antilog (E/S) versus the volume of the five additions of standard sulfamethoxazole. From the equation of the calibration curve the volume (mL) at intercept with X axis for the curve was calculate. The volume at intercept with X axis, concentration of the unknown sample (C_U), the analysis results are listed in Table 3-13.

Vol.(mL) of std. add	E/(mV)	Antilog (E/S)
0	130	168.559
0.5	134.97	205.060
1.0	138.69	237.466
1.5	142.37	274.559
2.0	144.92	303.608
2.5	147.75	339.460

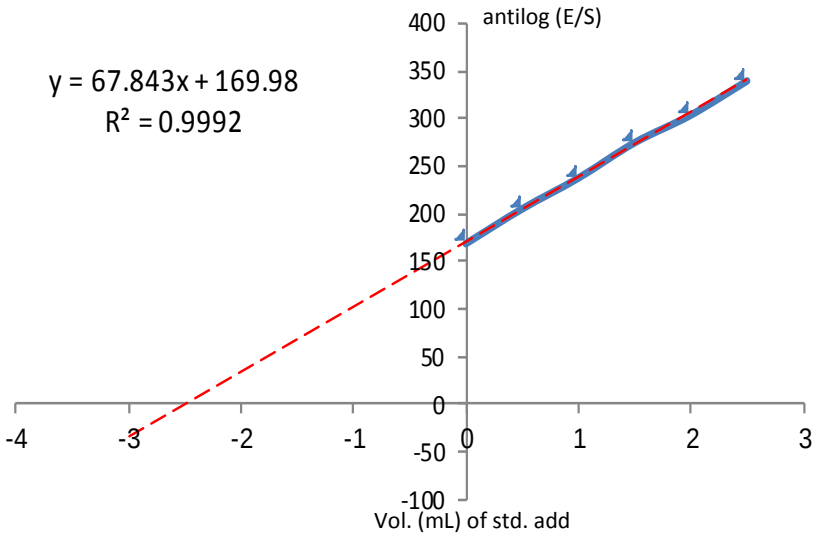


Figure 3-18:- Calibration curve of antilog (E/S) versus the volume added of standard 10^{-3}M for determination of 25 mL standard solution 10^{-4}M by (MSA) for E2 electrode.

Table 3-13:- The linear equation of the calibration curve uses MSA, correlation coefficient, volume at intercept, concentration of sample (C_U), Re% and E_r % of the unknown sample.

Linear equation	R	Volume at intercept (mL)	C_U(M)	Re%	E_r%
Y=67.843x+169.98	0.9992	2.505	1.002×10^{-4}	100.2%	0.2%

3-1-6-4-Titration method for drug:-

The potentiometric titration for 15 mL of 10^{-4}M sulfamethoxazole sample solution with 10^{-4}M of sodium tetraphenyl borate as titrant solution as shown in Figure 3-19 (a and b) the results of titration (Re%, E_r% and RSD%) are listed in Table 3-14.

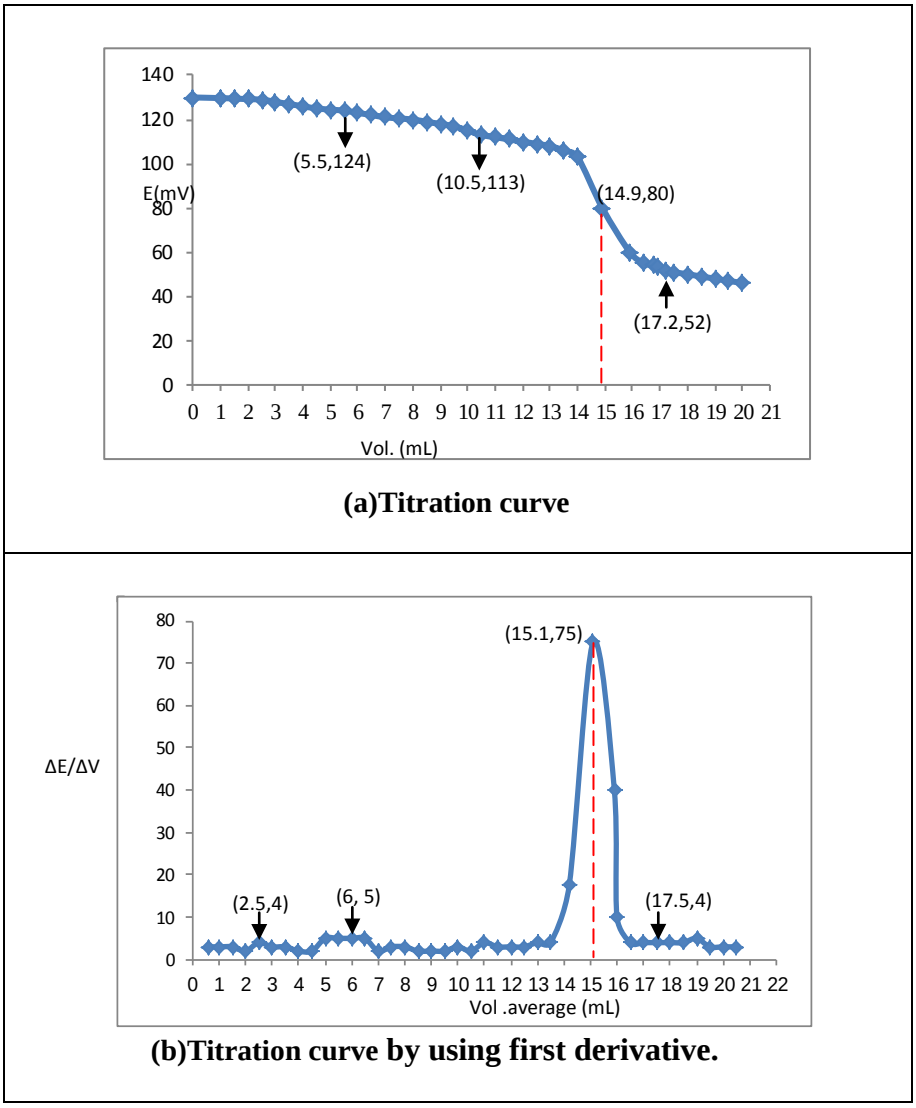


Figure 3-19 (a and b): Titration curve of E2, 15 mL sample solution 1×10-4 M sulfamethoxazole with 1×10-4M of (NaTPB) as a titrant solution.

Table 3-14:- The results of using titration method for E2 electrode for standard solution.

Titration Figure (3-19)	Vol. mL at the end point	C_U(M)	Re%	E_r %	RSD*%
Figure (a)	14.9	0.993×10^{-4}	99.3%	-0.7%	0.919%
Figure (b)	15.1	1.006×10^{-4}	100.6 %	0.6 %	

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

3-1-6-5-Analyses pharmaceutical preparations via electrod (E2):-

Electrode (E2) was proved to be useful in the potentiometric determination of sulfamethoxazole, Therefore it was used for the determination of the drug in pharmaceutical preparations and the data obtained for pharmaceutical samples were listed in Table 3-15.

Table 3-15:- Analyses of SMZ in pharmaceutical samples.

Parameter	*Direct method**	*SAM**	*Multi SAM**	*Titration method***
Conc.(M)	1.000×10^{-4}	1.000×10^{-4}	1.000×10^{-4}	1.000×10^{-4}
Found(M)	0.998×10^{-4}	0.998×10^{-4}	1.002×10^{-4}	0.999×10^{-4}
RSD*%	0.647%	0.885%	---------	0.919%
Re%	99.820%	100.980%	100.200%	99.95%
Er%	-0.180%	-0.360%	0.200%	-0.05%
δ_{n-1}	6.457×10^{-7}	8.820×10^{-7}	---------	9.192×10^{-7}
$\bar{x} \pm (ts/\sqrt{N})$	$0.998\times10^{-4}\pm0.779\times10^{-6}$	$0.998\times10^{-4}\pm 0.779\times10^{-6}$	---------	$0.999\times10^{-4}\pm0.825\times10^{-5}$

RSD% for n=2, t=12.7.***
RSD*% for n=5, t=2.7.

3-2-(Sulfamethoxazole-Sodium tetraphenyl borate) electrodes:-

3-2-1- FTIR spectrum of pure sulfamethoxazole and complex (sulfamethoxazole-sodium tetraphenylborate):-

The FTIR spectrum of the complex was compared with the reference spectrum of sulfamethoxazole， Fig.(3-20)(a and b). the spectra were shown in Table (3-16) .The value of N-H bond change from 3463 to 3199 that means the mono bond between SMZ and NaTPB and some bonds still the same with little changes.

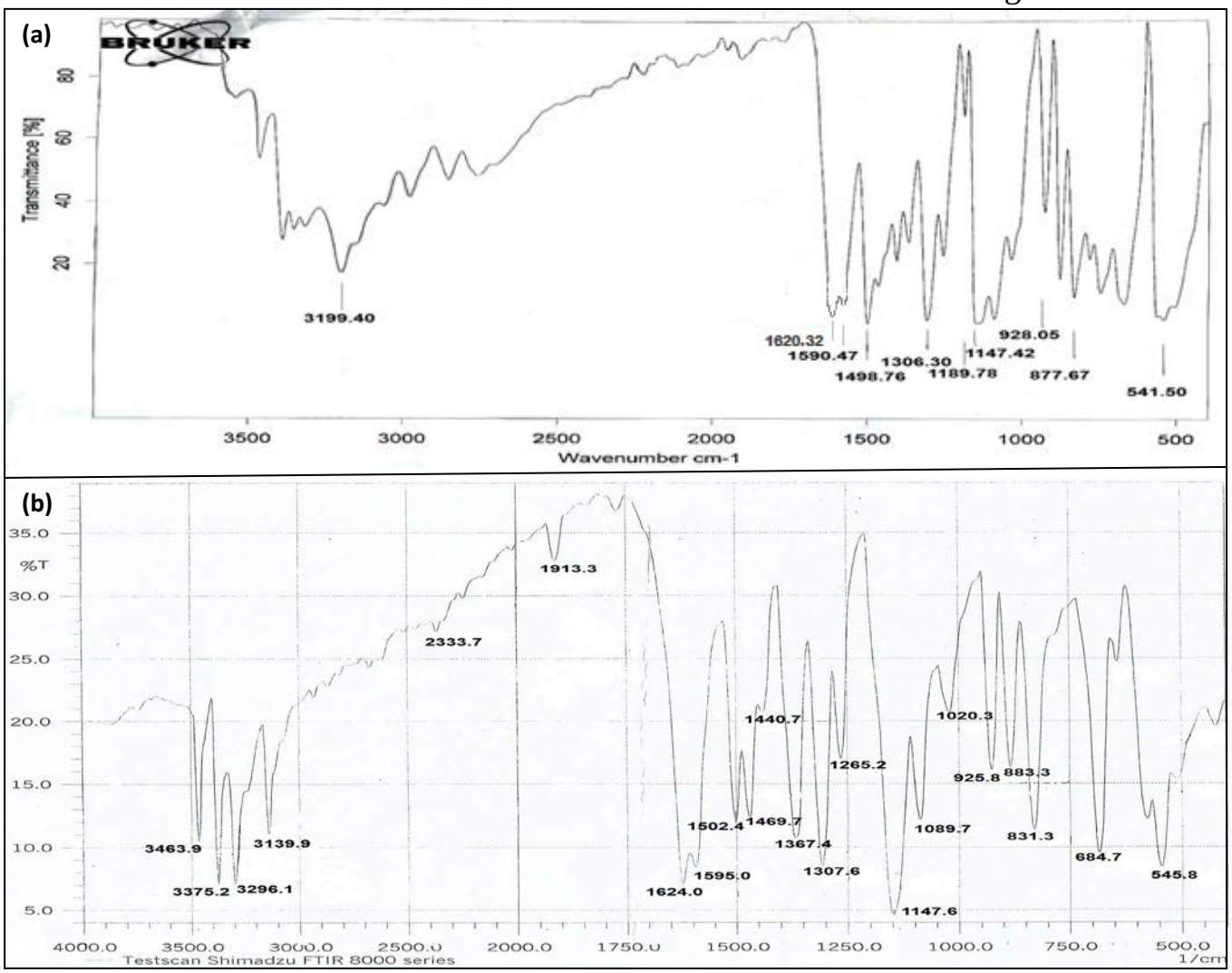


Fig. (3-20):a- FTIR spectrum of complex (SMZ-NaTPB).
b- FTIR reference spectrum of pure SMZ.

Table 3-16:- The functional groups obtained from the spectrum for pure sulfamethoxazole and sulfamethoxazole-sodium tetra phenyl borate complex.

Functional groups	Sulfamethoxazole(SMZ) cm^{-1}	Complex [SMZ-NaTPB] cm^{-1}
ν (N-H)	3463	3199
ν (S=O)	1307	1306
Bending (N-H)	1595	1590
ν (N=C)	1624	1620

3-2-2- Characteristics of (L1, L2, L3, L4, L5 and L6) electrodes:-

L1, L2, L3, L4, L5 and L6 were six ion selective electrodes based on using sulfamethoxazole-sodium tetraphenyl borate (SMZ-NaTPB) using six plasticizers: Tri-butyl phthalate (TBPH); Nitrobenzene (NB); Tri-butyl phosphate (TBP); Acetophenone (AP) ; Di-octyl phthalate (DOPH) and Ortho-nitro phenyl octyl ether (ONPOE) in PVC matrix were examined. Sulfamethoxazole selective electrodes (L1, L2, L3, L4 , L5and L6) which their calibration curves shown in Figure 3-21(a, b, c, d, e and f) respectively. The effects of different plasticizers were studied with respect to the linear range of concentration, slope, detection limit, response time and lifetime of the measured electrode as in table (3 - 17).

These electrodes gave the linear range from ($1x10^{-5}$-$1x10^{-2}$, $1x10^{-5}$-$1x10^{-2}$, $1x10^{-5}$-$1x10^{-2}$, $1x10^{-5}$-$1x10^{-2}$,$1x10^{-5}$-$1x10^{-2}$and $1x10^{-5}$-$1x10^{-2}$ M) and gave the slopes of (53.609, 49.608, 56.810, 55.709 , 50.808 and 51.808 mV/decade), with detection limit ($9x10^{-6}$ M, $8.5x10^{-6}$ M, $8x10^{-6}$ M, 8.9×10^{-6}M ,$7.5x10^{-6}$ and $7x10^{-6}$ M) respectively. The results were summarized in Table 3-17. The best electrode

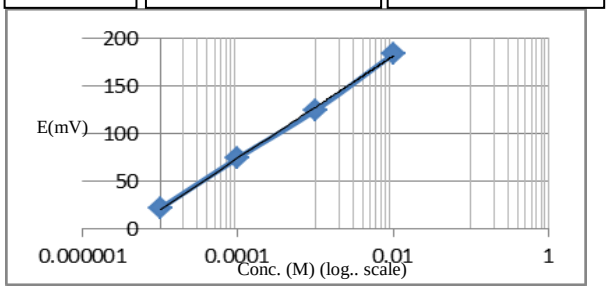
L3 (SMZ-NaTPB-TBP) which gives the Nernst slope 56.810mV/decade and correlation coefficient 0.9998, because the high mixing between the (TBP) and the complex.

Table 3-17:- The equation of calibration curves, slope, correlation coefficient, linear range, detection limit, response time and lifetime for sulfamethoxazole electrodes.

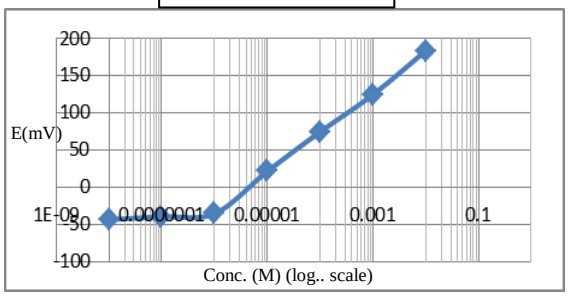
Electrode	Linear equation	Correlation coefficient (r)	Slope mV/Decade	Linear range (M)	Detection limit (M)	Response time (sec)			Life time (day)
						10^{-2}(M)	10^{-3}(M)	10^{-4} (M)	
L1 SMZ + NaTPB +TBPH	y = 23.278Ln(x) + 289.1	0.9994	53.609	1×10^{-2}– 1×10^{-5}	9×10^{-6}	12	16	29	12
L2 SMZ + NaTPB +NB	y = 21.541 Ln(x) + 219.1	0.9998	49.608	1×10^{-2}– 1×10^{-5}	8.5×10^{-6}	9	14	34	6
L3 SMZ + NaTPB +TBP	y = 24.668 Ln(x) + 266.8	0.9998	56.810	1×10^{-2}– 1×10^{-5}	8×10^{-6}	16	24	39	24
L4 SMZ + NaTPB +AP	y = 24.19Ln(x) + 221.7	0.9994	55.709	1×10^{-2}– 1×10^{-5}	8.9×10^{-6}	11	19	24	17
L5 SMZ + NaTPB +DOPH	y = 22.062Ln(x) + 253.8	0.9992	50.808	1×10^{-2}– 1×10^{-5}	7.5×10^{-6}	10	16	14	26
L6 SMZ + NaTPB +o-NPhOE	y = 22.496 Ln(x) + 262.8	0.9986	51.808	1×10^{-2}– 1×10^{-5}	7×10^{-6}	13	20	17	7

(a)

S=53.609 | SMZ+ NaTPB+TBPH | Y=23.278In(x)+289.1, r =0.9994

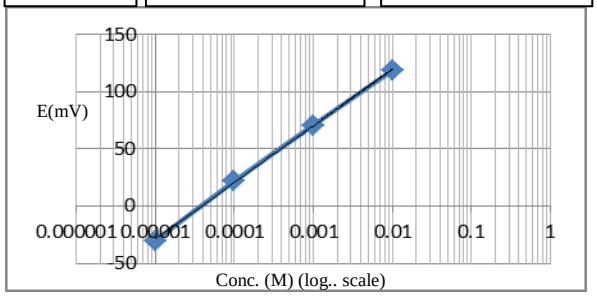


SMZ+NaTPB+TBPH

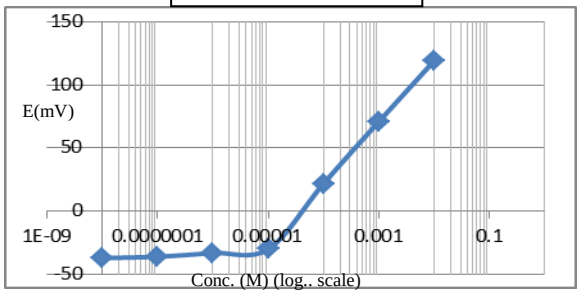


(b)

S=49.608 | SMZ+ NaTPB +NB | Y=21.541In(x)+219.1, r =0.9998

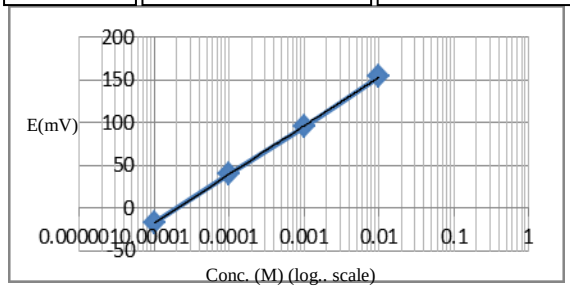


SMZ+ NaTPB +NB

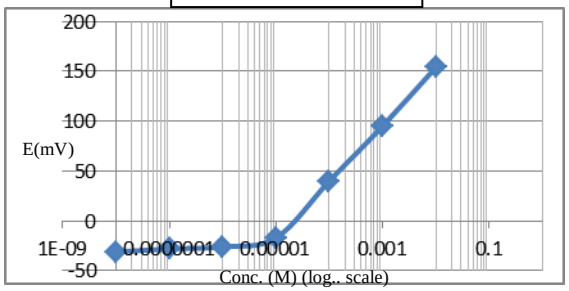


(c)

S=56.810 | SMZ+ NaTPB +TBP | Y=24.668In(x)+266.8, r =0.9998

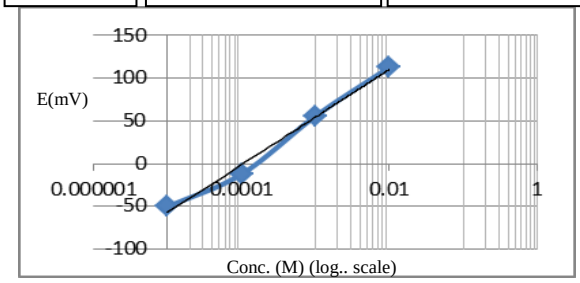


SMZ+ NaTPB +TBP

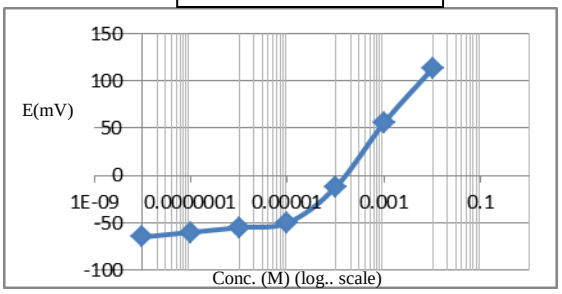


(d)

S=55.709 | SMZ+ NaTPB +AP | Y=24.19In(x)+221.7, r =0.9994



SMZ+ NaTPB +AP



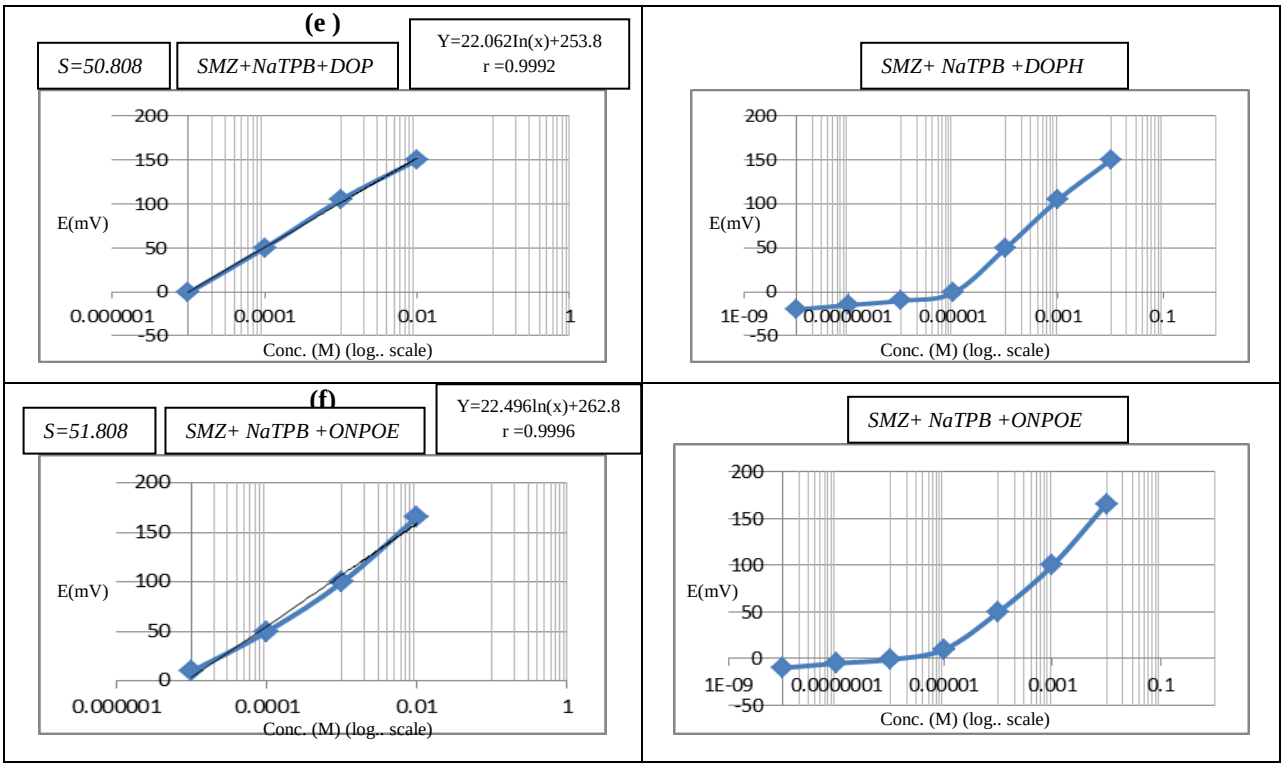


Figure 3-21:-The calibration curves of sulfamethoxazole electrodes were using different plasticizers: a-L1 electrode, b-L2 electrode, c-L3 electrode, d-L4 electrode, e-L5 electrode and f- L6 electrode.

From the results obtained, the L3 electrode was considered to be more sensitive than the other electrodes because of the slope value compared with slope value than the other electrodes. The L2 electrode gave non-Nernst slope, this could be due to the low viscosity of NB (1.863 cst) which causes rapid leaching of the complex out of the membrane when it is in contact with aqueous solution.

3-2-3-Effect of pH using L3 electrode:-

The pH adjusted by adding few drops of approximately 0.1 of hydrochloric acid and/or sodium hydroxide solution. Three different concentrations (1×10^{-2}, $1\times10^{-3}$and 1×10^{-4}) M were used to examine the effect of pH on the electrode potentials for SMZ selective electrode (L3) by measuring the potential of the cell in SMZ solutions in which the pH ranged from (0.5-11.0). The results shown in Fig.(3-22). At pH values less than 1.7 or in very high acidity, the electrode response has been increased rather irregularly, this may be due to that the electrode response to H_+ activities as well as SMZ ions, and in an alkaline solution (pH greater than 7) the electrode response has been decreased, this may be due to the formation of complexes of SMZ . The working pH were tabulated in Table (3-18).

Table 3-18:- Working pH ranges for Sulfamethoxazole L3 electrode.

Electrode no.	*Composition of electrode L3*	*pH range*		
		1×10^{-2} (M)	*1×10^{-3} (M)*	*1×10^{-4} (M)*
L3	**SMZ+NaTPB+ TBP**	**1.7-6.9**	**1.9-6.7**	**1.9-6.6**

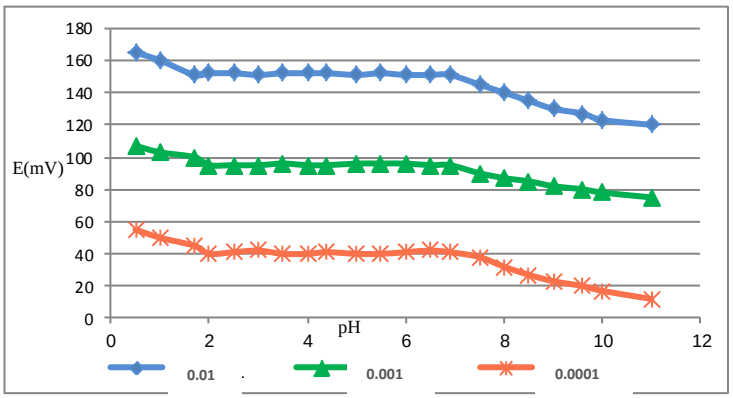


Figure 3-22:- Effect of pH on the potential of the L3 electrode at concentrations 10^{-2}, 10^{-3} and 10^{-4} M.

3-2-4-Selectivity methods using L3 electrode:-

3-2-4-1-Separate solution methods using L3 electrode:-

In the first case when ($a_A = a_B = 10^{-3}$ M) The potential is measured with two separate solutions, one containing the sulfamethoxazole at the concentration 10^{-3} M, the other one containing the interfering ion at the same concentration 10^{-3} M. The value of $K^{pot}_{A,B}$ is calculated by using the equation 1-9, by measurement the values of E_A and E_B. The results of selectivity coefficients are summarized in Table 3-19.

Table 3-19:- Selectivity coefficient values for L3 electrode, when E_A=95 mV and the slope 56.810 mV/decade.

Interfering Species	E_b	$logK^{pot}_{A,B}$	$K^{pot}_{A,B}$
Na^+	32	-1.108	7.78×10^{-2}
K^+	26	-1.214	6.10×10^{-2}
Cu^{2+}	11	-2.978	1.05×10^{-3}
Mn^{2+}	15	-2.908	1.23×10^{-3}
Fe^{3+}	12	-3.461	3.46×10^{-4}
Al^{3+}	10	-3.496	3.18×10^{-4}
Trimethoprim	34	-1.073	8.43×10^{-2}
Starch	9	-1.513	3.06×10^{-2}
Sucrose	7	-1.549	2.82×10^{-2}
Gelatin	5	-1.584	2.60×10^{-2}

From the Table 3-19, all values of $K^{pot}_{A,B}$ are less than (0.1), This reflects a very high selectivity of this electrode towards sulfamethoxazole.

3-2-4-2-Mixed methods (FIM) using L3 electrode:-

The potential of cell is measured for the solutions at constant concentration of the interfering ion (a_B) at first used (0.1) M that calculated in 20 mL total volume after mixed it with varying concentration of the sulfamethoxazole (a_A). The potential values obtained are plotted vs. the logarithm of the concentration of the sulfamethoxazole. The intersection of the extrapolated linear portions of this plot determination the value of (a_A). from Figure 3-23 to Figure 3-32can be used to calculate $K^{pot}_{A,B}$, all results of $K^{pot}_{A,B}$ were listed in Table 3-20.

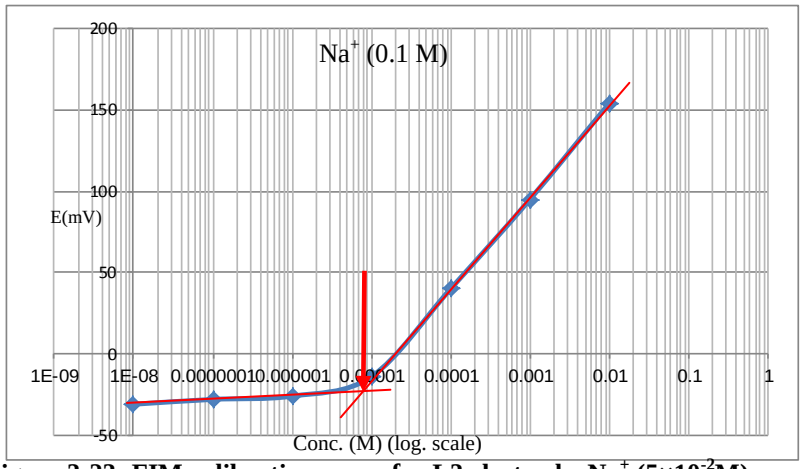


Figure 3-23: FIM calibration curve for L3 electrode, Na^+ (5×10^{-2}M) as interfering ion $a_A = 8.5\times10^{-6}$M.

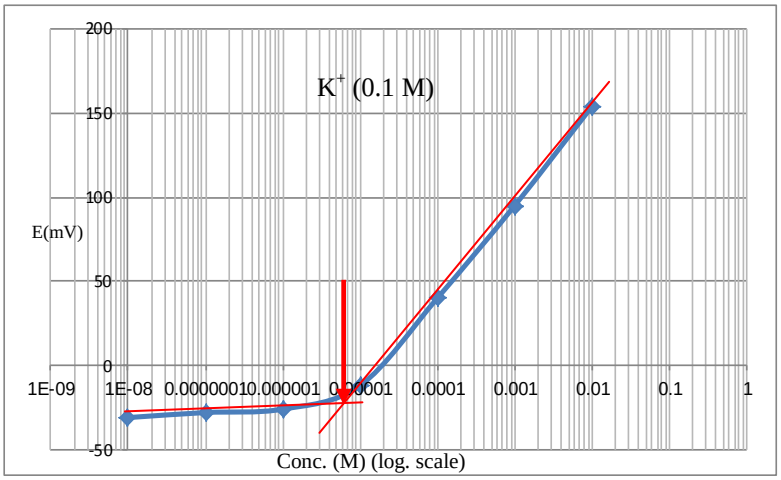


Figure 3-24: FIM calibration curve for L3 electrode, k^+ (5×10^{-2}M) as interfering ion $a_A = 6.7\times10^{-6}$M.

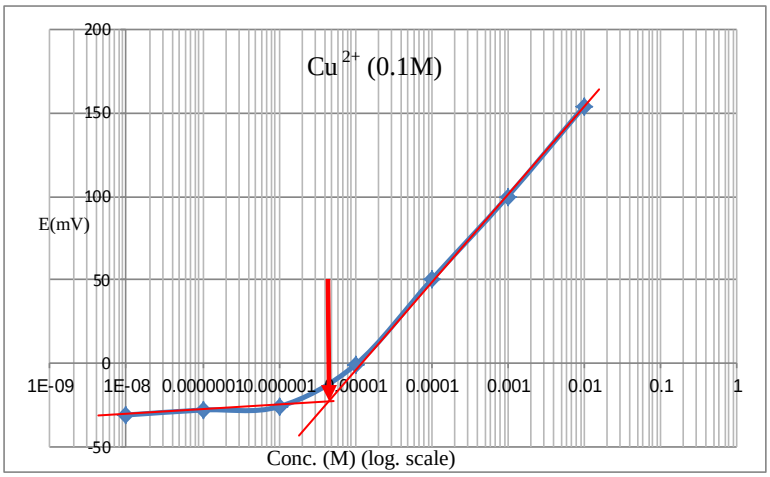


Figure 3-25: FIM calibration curve for L3 electrode, Cu^{2+} (5×10^{-2}M) as interfering ion $a_A = 5\times10^{-6}$M.

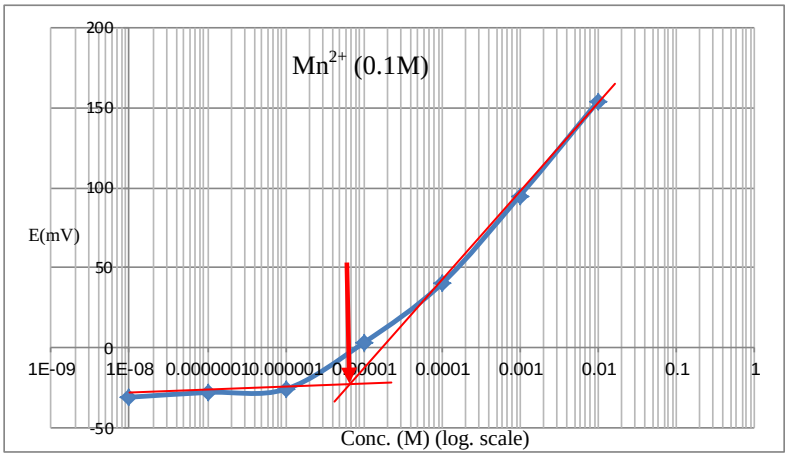


Figure 3-26: FIM calibration curve for L3 electrode, Mn^{2+} (5×10^{-2}M) as interfering ion $a_A = 6\times10^{-6}$M.

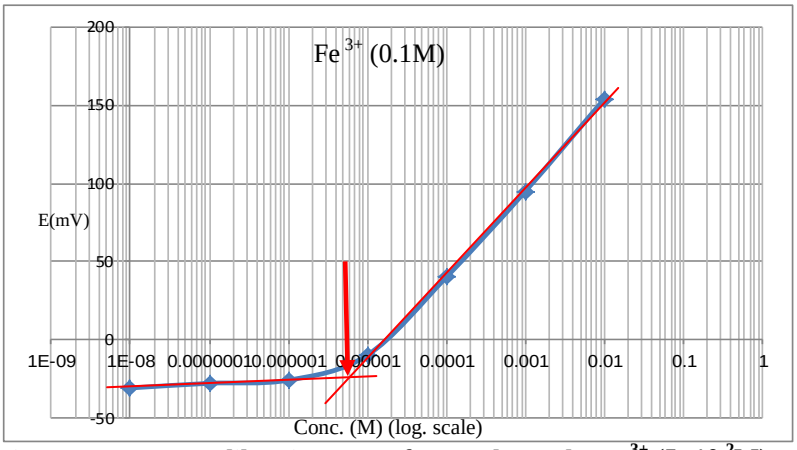


Figure 3-27: FIM calibration curve for L3 electrode, Fe^{3+} (5×10^{-2}M) as interfering ion $a_A = 5.5\times10^{-6}$M.

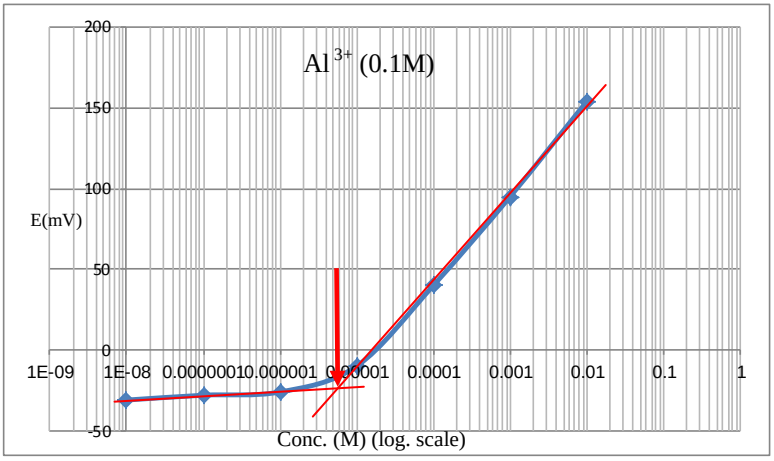


Figure 3-28: FIM calibration curve for L3 electrode, Al^{3+} (5×10^{-2}M) as interfering ion $a_A = 5.7\times10^{-6}$M.

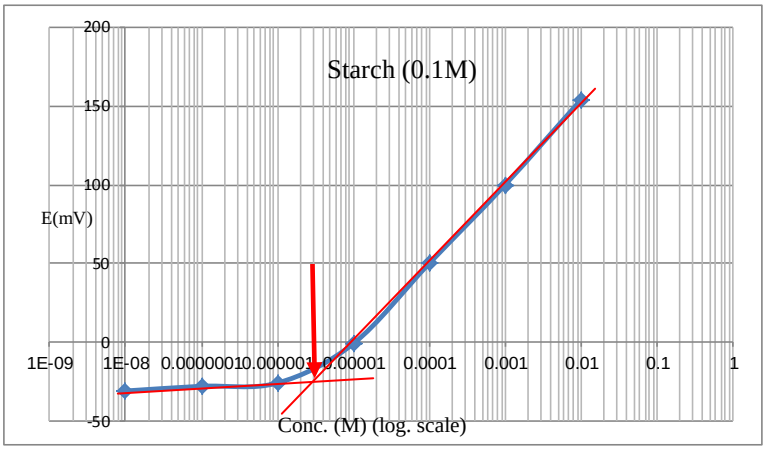


Figure 3-29: FIM calibration curve for L3 electrode, starch (5×10^{-2}M) as interfering ion $a_A = 3\times10^{-6}$M.

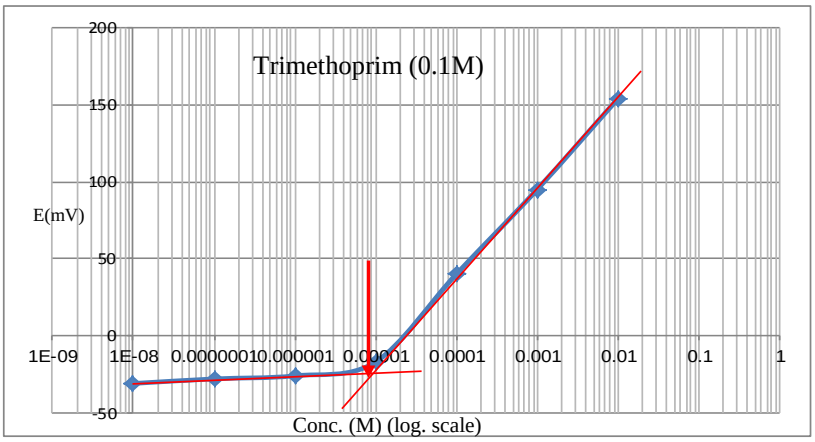


Figure 3-30: FIM calibration curve for L3 electrode, trimethoprim(5×10^{-2}M) as interfering ion $a_A = 9\times10^{-6}$M.

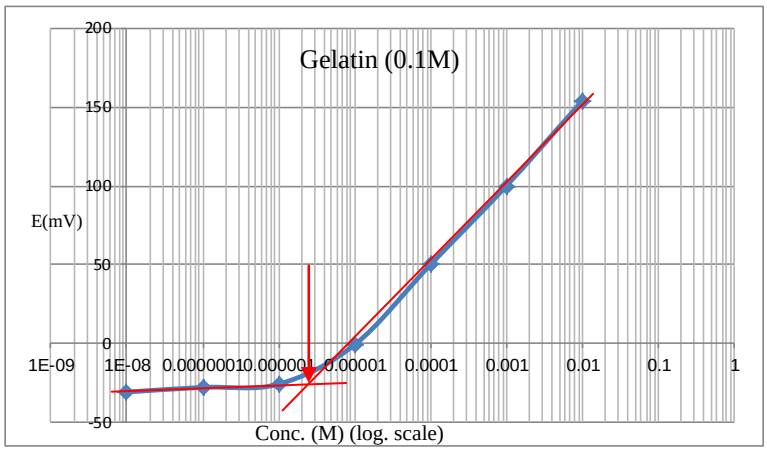


Figure 3-31: FIM calibration curve for L3 electrode, gelatine(5×10^{-2}M) as interfering ion $a_A=2.6\times10^{-6}$M.

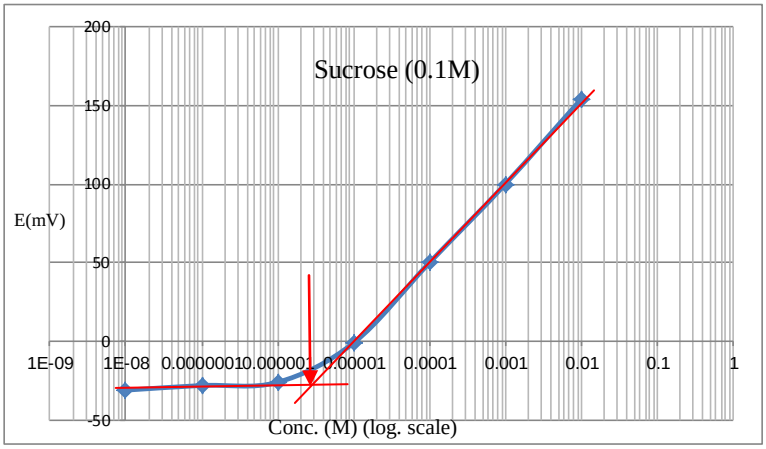


Figure 3-32: FIM calibration curve for L3 electrode, sucrose(5×10^{-2}M) as interfering ion $a_A=2.8\times10^{-6}$M.

Table 3-20:- Values of $K^{pot}_{A,B}$ according to FIM, *when* $a_B = 5\times10^{-2}$ M.

Interfering ions	$a_b = 5\times10^{-2}$	
	a_a	$K^{pot}_{A,B}$
Na^+	8.5×10^{-6}	1.7×10^{-4}
K^+	6.7×10^{-6}	1.3×10^{-4}
Cu^{2+}	5.0×10^{-6}	2.2×10^{-5}
Mn^{2+}	6.0×10^{-6}	2.6×10^{-5}
Fe^{3+}	5.5×10^{-6}	1.5×10^{-5}
Al^{3+}	5.7×10^{-6}	1.5×10^{-5}
Trimethoprim	9×10^{-6}	1.8×10^{-4}
Starch	3.0×10^{-6}	6.0×10^{-5}
Sucrose	2.8×10^{-6}	5.6×10^{-5}
Gelatin	2.6×10^{-6}	5.2×10^{-5}

3-2-5-Sample analyses using L3 electrode:-

3-2-5-1-Direct method of L3 electrode:-

The calibration curve was constructed for L3 electrode, as shown in Fig.3-33, and the concentration of the unknown was calculated from the linear equation y=24.668Ln(x) + 266.8 of the calibration curve which has the slope S =56.810 mV/decade and the intercept = 266.8, for n=5, the results are listed in table 3-21.

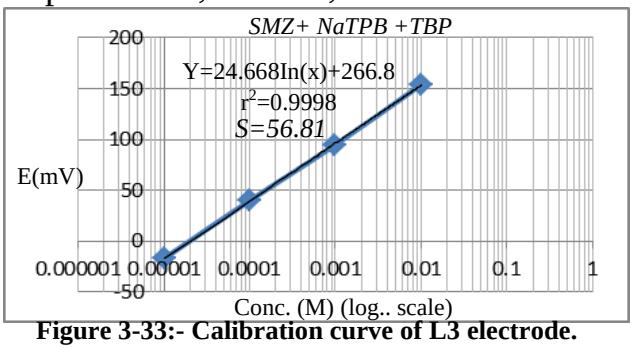


Figure 3-33:- Calibration curve of L3 electrode.

Table 3-21:- The results of six samples of sulfamethoxazole standard solution 10^{-4} M using direct method for L3 electrode, where slope=56.810 mV/decade.

Potential reading E(mV)	conc. of (SMZ) sample calculated from linear equation/(M)	*δn-1**	$\overline{X} \pm (ts/\sqrt{N})$	Re%	E_r%	RSD%
39.42	0.992×10^{-4}	9.354×10^{-7}	$0.988 \times 10^{-4} \pm 0.113 \times 10^{-5}$	99.2%	-0.8%	0.946%
39.07	0.978×10^{-4}			97.8%	-2.2%	
39.11	0.980×10^{-4}			98.0%	-2%	
39.64	1.001×10^{-4}			100.1%	0.1%	
39.33	0.989×10^{-4}			98.9 %	-1.1%	

δn-1*: at t=2.78 for N=5.

3-2-5-2-Standard additions method (SAM) of L3 electrode:-

It carried out by a procedure that 0.5 mL increment of 10^{-3}M sulfamethoxazole as standard was added to 25 mL of sample as unknown. The results of calculation (SAM) for the sulfamethoxazole using (L3) electrode and equation 1-13, recovery, relative error and relative standard deviation for five additions of sulfamethoxazole are listed in Table 3-22.

Table 3-22:- The results for five additions of sulfamethoxazole standard solution using (SAM) for L3 electrode, where slope=56.810 mV/decade, at concentration of sample 10^{-3} M.

V_S (mL) added	E/(mV)	ΔE	(V_U/V_S)	Antilog (ΔE/S)	C_U/(M)	*δn-1**	$\overline{X} \pm (ts/\sqrt{N})$	Re%	E_r %	RSD%
0	39	--------	∞	--------	----------	3.563×10^{-7}	$0.983\times10^{-4}\pm0.43\times10^{-6}$	----------	----------	0.362%
0.5	43.63	4.63	50	1.2064	0.982×10^{-4}			98.2%	-1.8%	
1.0	47.21	8.21	25	1.3948	0.989×10^{-4}			98.9%	-1.1%	
1.5	50.76	11.76	16.66	1.6106	0.980×10^{-4}			98.0%	-2%	
2.0	53.91	14.91	12.5	1.8300	0.981×10^{-4}			98.1%	-1.9%	
2.5	55.64	16.64	10	1.9629	0.984×10^{-4}			98.4	-1.6	

δn-1*: at t=2.78 for N=5.

3-2-5-3-Multi standard addition method (MSA)of L3 electrode:-

The calibration curve for MSA for (L3) electrode was shown in Figure 3-34 by plotting antilog (E/S) versus the volume of the five additions of standard sulfamethoxazole. From the equation of the calibration curve the volume (mL) at intercept with X axis for the curve was calculate. 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 3-23.

Vol.(mL) of std. add	E/(mV)	Antilog (E/S)
0	39	4.858
0.5	43.63	5.861
1.0	47.21	6.776
1.5	50.76	7.825
2.0	53.91	8.891
2.5	55.64	9.536

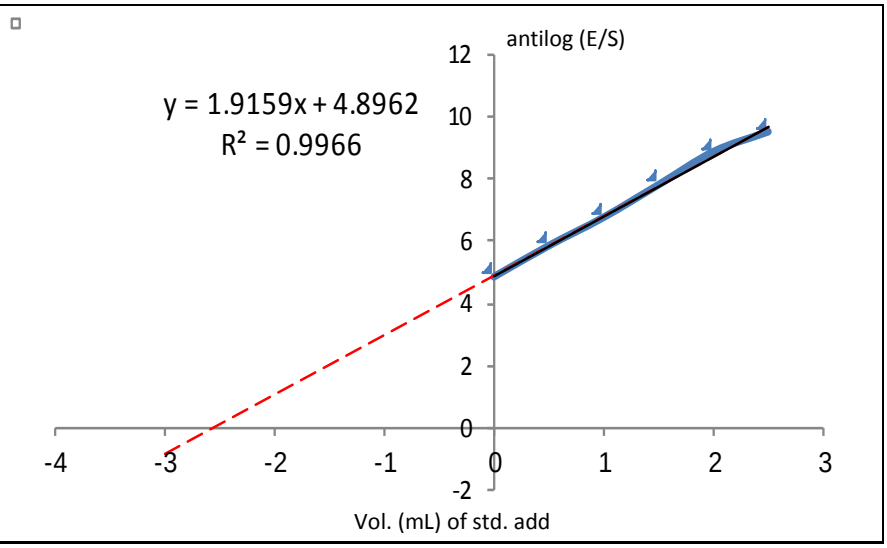


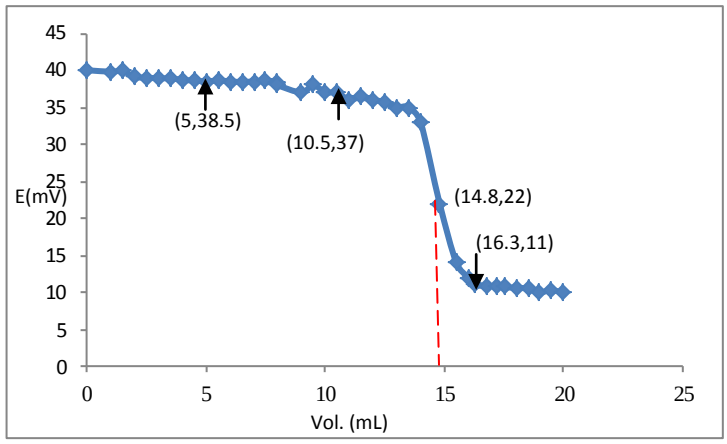
Figure 3-34:- Calibration curve of antilog (E/S) versus the volume added of standard 10^{-3}M for determination of 25 mL sulfamethoxazole solution 10^{-4}M by (MSA).

Table 3-23:- 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.

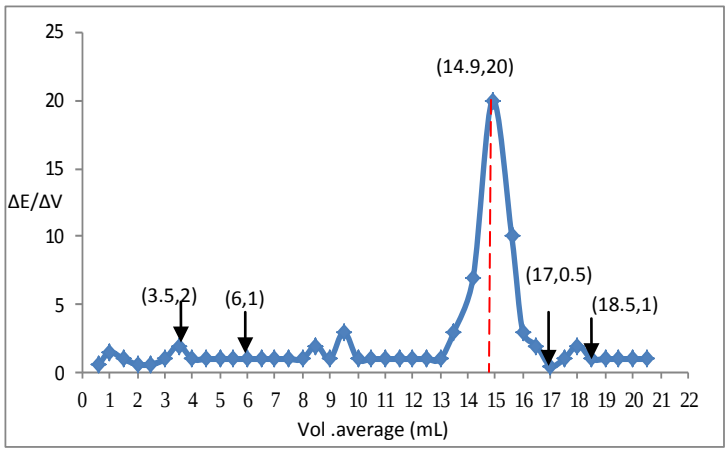
Linear equation	R	Volume at intercept (mL)	C_U(M)	Re%	E_r %
Y= 1.9159x+4.8962	0.9966	2.555	1.022×10^{-4}	102.2%	2.2%

3-2-5-4-Titration method of L3 electrode:-

The potentiometric titration for 15 mL of 10^{-4} M sulfamethoxazole sample solution with 10^{-4} M sodium tetraphenyl borate as titrant solution as shown in Figures 3-35(a and b) , the results of titration (Re%, E_r% and RSD%) are listed in Table 3-24.



(a) Titration curve



(b) Titration curve by using first derivative.

Figure 3-35(a and b): Titration curve of L3, 15mL sample solution 1x10^{-4}M sulfamethoxazole with 1x10^{-4}M of NaTPB as a titrant solution

Table 3-24:-The results of using titration method for standard sulfamethoxazole sample for L3 electrode.

Titration Figure (3-35)	Vol. mL at the end point	C_U(M)	Re%	E_r%	RSD*%
Figure (a)	14.8	0.986×10^{-4}	98.6 %	-1.4 %	0.476%
Figure (b)	14.9	0.993×10^{-4}	99.3%	-0.7%	

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

the data obtained for L3 electrode using direct method, standard addition method, multi standard addition method and titration method were listed in Table 3-25.

Table 3-25:- Analysis of SMZ by potentiometric techniques by using ISE L3.

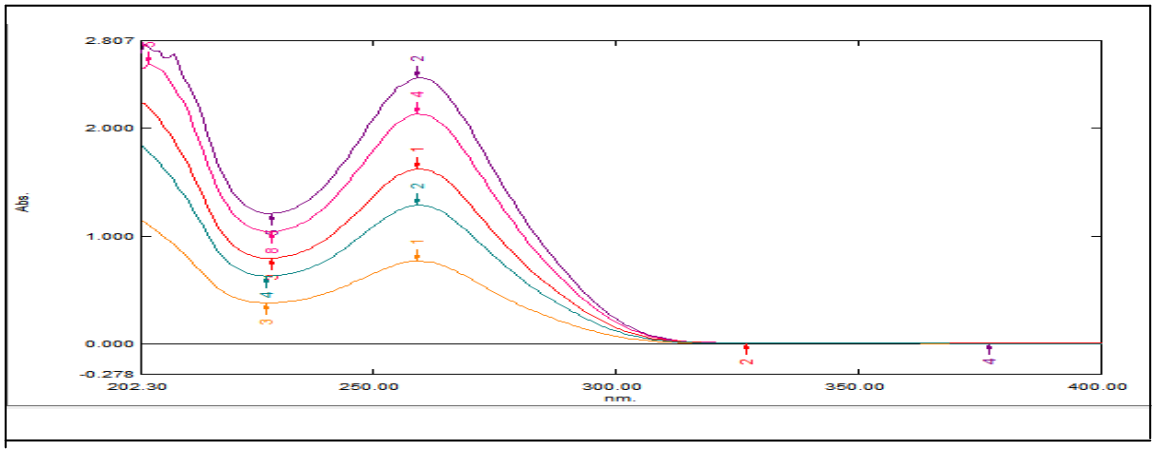
Parameter	Direct method*	SAM*	Multi SAM*	Titration method***
Conc.(M)	1.000×10^{-4}	1.000×10^{-4}	1.000×10^{-4}	1.000×10^{-4}
Found(M)	0.988×10^{-4}	0.983×10^{-4}	1.022×10^{-4}	0.989×10^{-4}
RSD*%	0.946%	0.362%	---------	0.476%
Re%	98.800%	98.320%	102.200%	98.999%
Er%	-1.200%	-1.68%	2.200%	-1.001%
δ_{n-1}	9.354×10^{-7}	3.563×10^{-7}	---------	4.716×10^{-7}
$\bar{x} \pm (ts/\sqrt{N})$	$0.988\times10^{-4}\pm0.112\times10^{-5}$	$0.983\times10^{-4}\pm0.43\times10^{-6}$	---------	$0.989\times10^{-4}\pm0.423\times10^{-5}$

RSD% for n=2, t=12.7.***
RSD*% for n=5, t=2.7.

3-2-6- Spectrophotometry :-

3-2-6-1-Normal spectra :-

Fig.(3-36) shows the normal spectra for sulfamethoxazole solutions ($0.990x10^{-4}$, $0.996x10^{-4}$, $0.999x10^{-4}$, $1.004x10^{-4}$, $1.005x10^{-4}$) M , the absorption wavelength at 259.00 nm.



Figure(3-36):- The normal spectra for SMZ solutions.

The calibration curve were constructed for the wavelengths (259.00) nm as shown in Figures 3-37

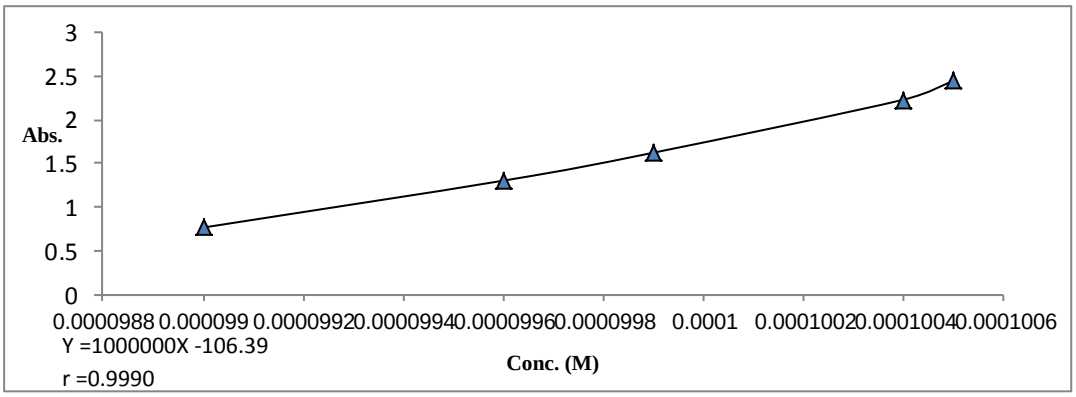


Figure (3-37):- Calibration curve of normal spectrum for SMZ at λ 259.00 nm.

Figure 3-37 shows the calibration curve of normal spectram at the λ 259.00 nm, from the linear equation of the calibration curve (y = 1000000 x -106.39) the concentration of sulfamethoxazole can be calculated . The results of sulfamethoxazole are listed in Table 3-26.

Table 3-26:-Calculation for five samples of $10^{-4}$of SMZ standard solution by using direct method for calibration curve of normal spectram of UV-spectrophotometry at λ (259.00 nm).

Abs.	*Conc. (M)*	*δn-1**	$\bar{X} \pm (ts/\sqrt{N})$	*Re%*	E_r%	RSD%
0.764	0.990 x 10^{-4}	6.1400 x 10^{-7}	$0.998x10^{-4} \pm 0.763x10^{-6}$	99.00%	-1%	0.6152%
1.301	0.996 x 10^{-4}			99.60%	-0.4%	
1.621	0.999 x 10^{-4}			99.90%	-0.1%	
2.128	1.004 x 10^{-4}			100.40%	0.4%	
2.466	1.005 x 10^{-4}			100.50%	0.5%	

δn-1*: at t=2.78 for N=5.

The calculated linear equation for normal spectram, correlation coefficient and concentration are listed in Table 3-27.

Table(3-27):- Calculation linear equations, correlation coefficient and the range of concentrations for the normal spectrum.

Method	λ(nm)	*Concentration(M)*	*Linear equation*	*(r) Correlation Coefficient*
Normal spectram	259.00	1.06 x 10^{-4}	y = 1000000 x -106.39	0.9990

3-2-7-Comparison between ISE and normal spectrum methods:

The comparison between normal spectrum and direct method of ion selective electrode by using F-test using 95% confidence level are shown in the Table 3-28.

Table (3-28):- Calculation of F-test between the two methods ISE and normal spectra.

CU(M) from direct method of ISE	δ_{n-1}*	CU(M) from direct method of normal spectrum	δ_{n-1}*	The (F) magnitude
0.993×10^{-4}	4.098×10^{-7}	0.990×10^{-4}	6.140×10^{-7}	2.244
0.998×10^{-4}		0.996×10^{-4}		
0.992×10^{-4}		0.999×10^{-4}		
1.002×10^{-4}		1.004×10^{-4}		
0.998×10^{-4}		1.005×10^{-4}		

δn-1*: standard deviation; n= 5, F= S12 / S22, where S1 >S2 ,FTable=6.39.

$F_{calculate}$ less than F_{table}, we conclude that there is no difference in precision between two methods.

3-3- Conclusion :

Two types of electrodes were prepared in this study based on PVC matrix for (SMZ-TPA) and (SMZ-NaTPB)

Type one:- four ion selective electrodes included formation of membranes for sulfamethoxazole based on sulfamethoxazole and tungestophosphoric acid using six plasticizers: Di-butyl phthalate (DBPH), Di-octyl phthalate (DOP), Tri-butyl phosphate (TBP), Nitrobenzene (NB), Ortho-nitro phenyl octyl ether (ONPOE) and Acetophenone (AP) in PVC matrix membrane. The best electrode for sulfamethoxazole was (E2) electrode which used to determine sulfamethoxazole in the pharmaceutical sample (Trimole tablets), it also has the working pH in the range (1.6 – 6.8).

There is no interference for interference measurements with (Na^{+}, K^{+} Mn^{+2}, Cu^{+2}, Fe^{+3}, Al^{+3}, starch, sucrose , trimethoprim and gelatin). The practical utility of the electrode has been demonstrated by use it as indicator electrode in potentiometric precipitation titration of sulfamethoxazole solution with tungestophosphoric acid solution. Direct method, standard additions method and multi standar 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 normal spectrum spectroscopy.

Type two:- six ion selective electrodes included formation of membranes for sulfamethoxazole based on sulfamethoxazole and sodiumtetraphenylborate using six plasticizers: Di-butyl phthalate (DBPH), Di-octyl phthalate (DOP), Tri-butyl phosphate (TBP), Nitrobenzene (NB), Ortho-nitro phenyl octyl ether (ONPOE) and Acetophenone (AP) in PVC matrix membrane. The best electrode for sulfamethoxazole in the second type was (L3) electrode which used to determine sulfamethoxazole in pure sample . It also has the working pH in the range (1.7 – 6.9). Also there is no interference for interference measurements with (Na^{+}, K^{+}, Mn^{+2}, Cu^{+2}, Fe^{+3}, Al^{+3}, starch, sucrose , trimethoprim and gelatin). Direct method, standard additions method and multi standard additions method have been also successfully applied and showing a very good results. The practical utility of the electrode has been demonstrated by use it as indicator electrode in potentiometric precipitation titration of sulfamethoxazole solution with sodium tetraphenyl borate solution.

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

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

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

4- Application of these membranes in analyses of other drug samples with similar active groups.

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الخلاصة

في هذه الدراسة تم تحضير نوعين من الاقطاب الانتقائية اساسها من مادة البولي فاينيل كلورايد.
الاولى: اربعة اقطاب انتقائية للسلفاميثوكسازول والتي تعتمد على المعقد (سلفاميثوكسازول-تينكيستوفوسفوريك) كمادة فعالة تم تحضيرها.
الثانية: ستة اقطاب انتقائية للسلفاميثوكسازول ايضا والتي تعتمد على المعقد(سلفاميثوكسازول-صوديومتيترافانيل بوريت) كمادة فعالة وفي كلا النوعين تم استخدام المواد الملدنة الاتية:
Tri-butyl phthalate (TBPH); Nitrobenzene (NB); Tri-butyl phosphate (TBP); Acetophenone (AP); Di-octyl phthalate (DOPH); o-nitrophenyloctyleether (o-NPOE).
دراسة خواص الاقطاب والتي تتضمن (مدى التركيز الخطي، مقياس المعايرة، حد التحسس، زمن الاستجابة، عمر القطب ومدى الدالة الحامضية والانتقائية) وكذلك تطبيق المعالجة الاحصائية على هذه النتائج والتي تشمل(نسبة الانحراف القياسي ونسبة الخطا وحد الثقة للتراكيز). من خلال هذه النتائج نلاحظ: النوع الاول لاقطاب السلفاميثوكسازول الانتقائية:-
SMZ-TPA+DOPH (E1), SMZ-TPA+TBP (E2), SMZ-TPB+AP (E3) and SMZ-TPA+NB (E4), ومدى التركيز الخطي لها - (1×10^{-5}-1×10^{-2}, 1×10^{-7}-1×10^{-2}, 1×10^{-2}, 1×10^{-5}-1×10^{-2} and 1×10^{-5}-1×10^{-2} M) وحد تحسس ملفولت/حقبة (52.008, 58.381, 56.909 and 50.309) لها انحدارا (9×10^{-6}, 9×10^{-8}, 6×10^{-6} and 7×10^{-6})مولاري وزمن الاستجابة 30, 28, 36 and 25 ثانية لتركيز محلول 10^{-3} مولاري من السلفاميثوكسازول وعمر القطب 29, 27, 20 and 9) يوم . اما النوع الثاني لاقطاب السلفاميثوكسازول الانتقائية :-
SMZ-NaTPB+TBPH (L1), SMZ-NaTPB +NB (L2), SMZ-NaTPB +TBP (L3), SMZ-NaTPB +AP (L4), SMZ-NaTPB +DOPH (L5) and SMZ-NaTPB +o-NPhOE (L6)
مدى التركيز الخطي لها - (1×10^{-5}-1×10^{-2}, 1×10^{-5}-1×10^{-2}, 1×10^{-5}-1×10^{-2} , 1×10^{-2} , 1×10^{-5}-1×10^{-2} and 1×10^{-5}-1×10^{-2} M), وحد تحسس 7×10^{-6} , and 7.5×10^{-6} , 8.9×10^{-6}, 8×10^{-6}, 8.5×10^{-6}, 9×10^{-6}) لها انحدارا (53.609, 49.608, 56.810 , 55.709, 50.808 and51.808) ملفولت/حقبة مولاري وزمن الاستجابة (16, 14, 24, 19, 16 and 20) ثانية لتركيز محلول10^{-3} مولاري من السلفاميثوكسازول وعمر القطب (12, 6, 24, 17, 26 and 7) يوم .
لقد وجد ان افضل قطب من المجموعة الاولى هوE2 ومن المجموعة الثانية هو L3 الاثنان استخدما لتقدير السلفاميثوكسازول في النماذج النقية. لقد وجد ان مدى الدالة الحامضية للقطب E2 بحدود(1.6-6.8) وللقطب L3 بحدود (1.7-6.9) كذلك تم دراسة التداخلات لحساب معامل الانتقائية بطريقة المحاليل المنفصلة وطريقة المحاليل الممزوجة بوجود الايونات و المواد التالية (Na+, K+, Mn+, Cu+, Al+, Fe+, sucrose, starch, trimethoprim

and gelatin) . ان قطب E2 اعطى افضل نتائج مقارنة ببقية الاقطاب حيث استخدم لتقدير السلفاميثوكسازول في المستحضرات الصيدلانية باستخدام طرق القياسات الجهدية المختلفة .

كذلك استخدمت الدراسات الطيفية التي تتضمن الاطياف الاعتيادية لمحاليل السلفاميثوكسازول ($0.990x10^{-4}$, $0.996x10^{-4}$, $0.999x10^{-4}$, $1.004x10^{-4}$, $1.005x10^{-4}$) مولاري وبطول موجي يساوي 259.00 نانومتر. نتائج الطرق التحليلية بينت انها بسيطة، سريعة وبدقة عالية ولقد تمت مقارنة بين طريقة الاطياف الاعتيادية والطريقة المباشرة للاقطاب الانتقائية من خلال اجراء F-test والنتائج اظهرت انه لايوجد اختلاف بين الطريقتين لان نسبة القيمة العملية اقل من النظرية عند حد الثقة 95%.

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قسم الكيمياء

تحضير اقطاب بوليمرية جديدة للسلفاميثوكسازول واستخدامها في تحديد بعض الادوية

رسالة
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من قبل
سراء عبدالعزيز ابراهيم
بكالوريوس علوم كيمياء 2008 (جامعة النهرين)

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