Introduction

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

Ion selective electrodes (ISEs) are part of group of relatively simple and inexpensive analytical tools which are commonly referred to as sensors. The pH electrode is the most well known and simplest member of this group and can be used to illustrate the basic principles of ion selective electrodes [1]. Also, ISE is a transducer sensor which converts the activity of a specific ion dissolved in solution into an electrical potential which can be measured by a voltmeter or pH meter. The sensing part of the electrode is usually made as an ion specific membrane, along with a reference electrode. It is impossible to measure the interfacial potential directly, but this can be achieved using a suitable electrochemical cell and the potential is measured at equilibrium under a zero current condition [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 zeroth (inert metal in a redox electrolyte). 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.

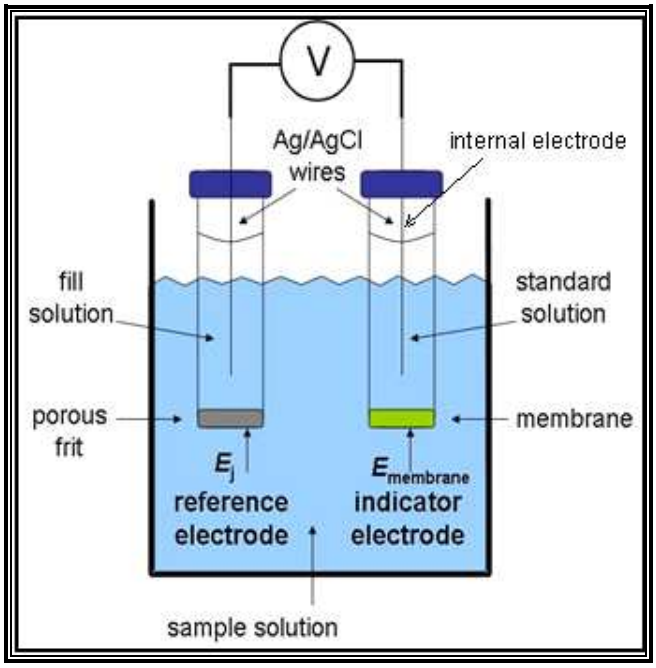


Figure 1-1:- A classical ion selective electrode in electrochemical cell [3].

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]:-

$$\mathbf{E = E^0 - (RT/nF) \ln a} \qquad \textbf{…1-1}$$

$$\mathbf{E = E^0 - (2.303RT/nF) \log a} \qquad \textbf{…1-2}$$

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:-

$$\mathbf{E = E^0 - (59.2 / n) \log a} \qquad \mathbf{\ldots 1\text{-}3}$$

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]

$$\mathbf{E_{total} = E^0 + E_{junction} - E_{membren}} \qquad \mathbf{\ldots 1\text{-}4}$$

1-3-Classification of ion selective electrode membranes:-

There are five types of ion selective membranes used in the construction of ISEs, these are:-

1-3-1-Crystalline membrane electrode:-

Solid state electrode has a membrane made up of a single crystal, for example, chloride selective electrode with a poly solid contact. The crystal lattice allows the anions to move freely within an immobile framework of cation, thus the ions do penetrate and move about the crystal lattice. The electrodes usually have a true Nernst response if the concentration is greater than 10^{-6} M. It becomes less accurate at very low concentrations by the finite solubility of the crystal. [6]

1-3-2-Glass membrane electrodes [7]:-

A glass electrode is a type of ion selective electrode and sensitive to a specific ion. All commercial electrodes respond to single charged ions,

like H^+, Na^+ and Ag^+. The most common glass electrode is the pH electrode. The components of glass electrode are:-

- A sensing part of electrode, a bulb made from a specific glass (e.g. a silicate glass as a membrane).
- Sometimes the electrode contains a small amount of AgCl precipitate inside the glass electrode. Internal solution, usually 0.1M HCl and internal electrode, usually silver chloride electrode or calomel electrode.
- Body of electrode, made from non-conductive glass or plastics.
- Reference electrode.

A typical modern pH cell as shown in Figure 1-2, is called the combined electrode, which contains both the glass and reference electrodes into one body. The inner tube contains an unchanging saturated KCl and 0.1 M HCl solution.[7]

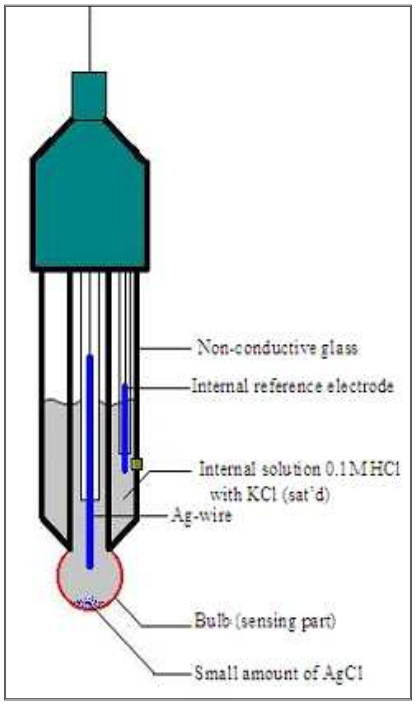


Figure 1-2:- A glass cell type [7].

1-3-3-Liquid membrane electrodes:-

This kind of membrane is usually the supported PVC matrix containing the ion exchanger or ionophore dissolved in a suitable solvent mediator (plasticizer). Without the exchanger or ionophore the ion of interest is unable to penetrate the membrane. [8]

A general rule is that PVC-based polymer membranes used for potentiometric sensors should contain about 70% by weight plasticizer and 30% PVC [9]. The role of the plasticizers is to lower the glass transition temperature of PVC in which a homogenous and flexible films with good mechanical stability are produced. The amount of ionophore needed is only about 1% and included in the amount of plasticizer. The main component of electro-active membrane is neutral or charged compounds, which is able to complex ions reversibly and to transfer them through an organic membrane by carrier translocation. This compound is called as an ionophore or an ion carrier. There are two kinds of ionophores: charged and neutral carriers. They are mobile in both free and complex forms, so the mobility of all species is part of the selectivity coefficient together with ion-exchange equilibrium. The mobile binding sites are dissolved in a suitable solvent and usually trapped in a matrix of organic polymer (gel). An appropriate plasticizer is added to a membrane in order to ensure the mobility of the free and complex ionophore. It determines the membrane polarity and provides suitable mechanical properties of membrane. Although other polymers like: polisiloxane, polystyrene, polyamide or polyimide can be used a membrane matrix, PVC is the most widely used matrix due to simplicity of membrane preparation. Examples of such ion selective electrodes are Ca^{+2} and NO_3^-. [10]

Accordingly, the choice of plasticizer has a great effect on the electrode properties such as; the response, linearity, slope and selectivity. The solvent mediator used to dissolve the ion-exchange sensor plays supplementary roles by adjusting:

- Ultimate relative permittivity of the final organic phase.
- Mobility of the ion-exchange sites according to the viscosity of the mediator.
- Site density by variation of the concentration of the ion exchanger.

These adjustments can influence the extent of synergistic enhancement of the partition coefficient for the ion with consequent effect on electrode selectivity. There are two types of this kind of electrodes [11]:-

a-Rigid self-supporting:- ion selective electrodes in which the sensing membrane is a thin polymer with fixed sites or a thin piece of glass. The chemical composition of the polymer for example, polystyrenesulfonate, sulfonated poly (tetrafluoroethylene), amino-poly (viny1chloride).

b-Electrodes with mobile charged sites:-

1- 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.

2-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.

3-Uncharged electrodes: - based on solutions of molecular complexing agents 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.

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

1-3-4-Gas 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. [12]

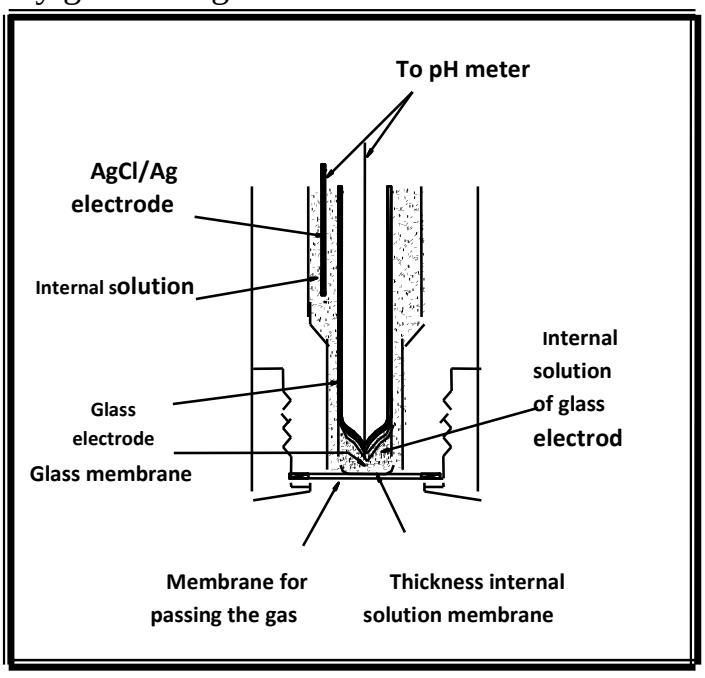


Figure 1-3:- A gas sensing electrodes type [12].

1-3-5-Enzyme electrodes:-

Enzyme electrodes definitely are not 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 is glucose selective electrodes. [13]

1-4-Reference electrodes:-

Reference electrodes are applicable in instances where the electrical potential is to be imposed or measured in a solution. Also, it has a stable and well defined electrochemical potential against which the applied or measured potentials in an electrochemical cell are referred. In order to measure the change in potential difference across the ion selective membrane as the ionic concentration changes, it is necessary to include in the circuit a stable reference voltage which acts as a half-cell from which to measure the relative deviations. [14]

1-4-1-Types of reference electrodes:-

1-4-1-1-Single junction reference electrode:- such as Ag/AgCl and Hg/Hg_2Cl_2. The saturated calomel reference electrode (SCE) is one such constant potential electrode. A typical SCE available commercially is shown in Figure 1-4-a. It consists of two glass tubes, which we will refer to here as an outer tube and an inner tube. The outer tube has a porous fiber plug in the tip which acts as the “salt bridge” to the analyte solution.

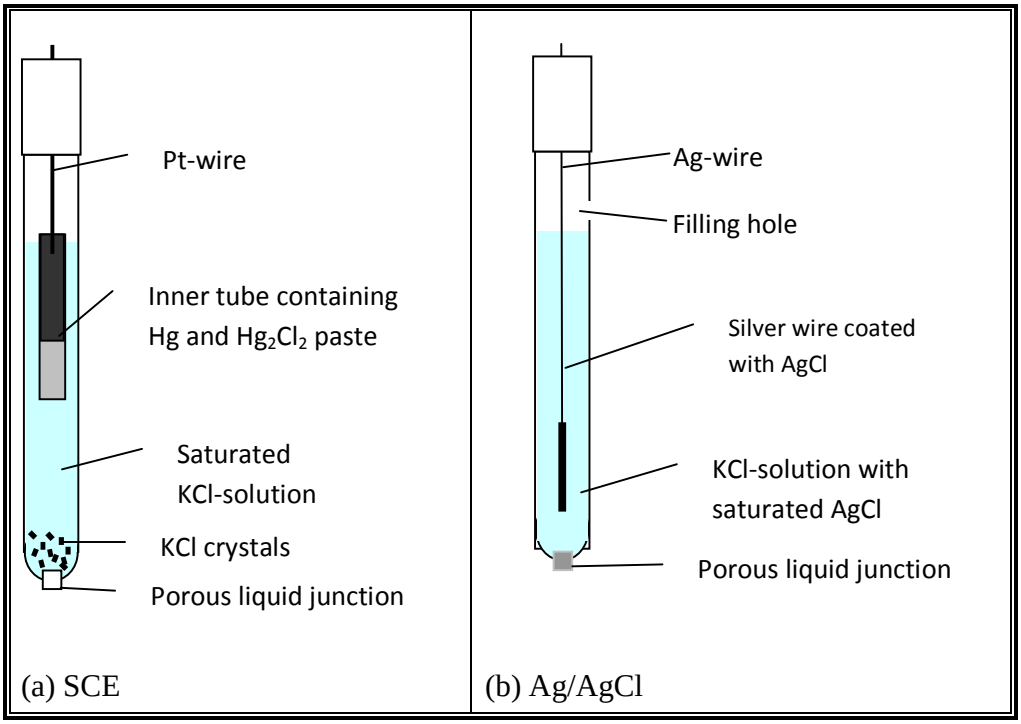


Figure 1-4:-Types of reference electrodes, (a)-SCE and (b)-silver-silver chloride [15].

A solution of potassium chloride is in the outer tube [15]. The electrode potential is equal +0.241volt versus standard hydrogen electrode at 25^0C. When in use the following half-cell reaction occurs:

$$\mathbf{Hg_2Cl_2 + 2e^- \leftrightarrow 2Hg + 2Cl^-}$$

The other type is Ag/AgCl, is the most widely used reference electrode. This electrode consists of silver-wire in contact with AgCl in a saturated KCl solution. A typical is shown in Figure 1-4-(b). The electrode potential is equal +0.197 volt versus standard hydrogen electrode at 25^0C. Most electrodes of this type use saturated KCl (3 M) as electrolyte.

$$\mathbf{AgCl + e^- \leftrightarrow Ag + Cl^-}$$

1-4-1-2-Double junction reference electrode [16]:-

It is preferable to use a double junction reference electrode for ISE applications. The standard reference half cells as shown in Figure 1-4, which based on KCl electrolyte filling solutions have a distinct disadvantage when; for example, potassium or chloride ion is being measured. To overcome this, a double junction reference as shown in Figure 1-5, is used in which the escaping KCI is retained in a second chamber containing a non-interfering electrolyte, which in turn escapes into the test solution. The filling solution for the inner chamber of a double junction reference electrode is 4M KCI saturated with AgCl for a silver/silver chloride electrode.

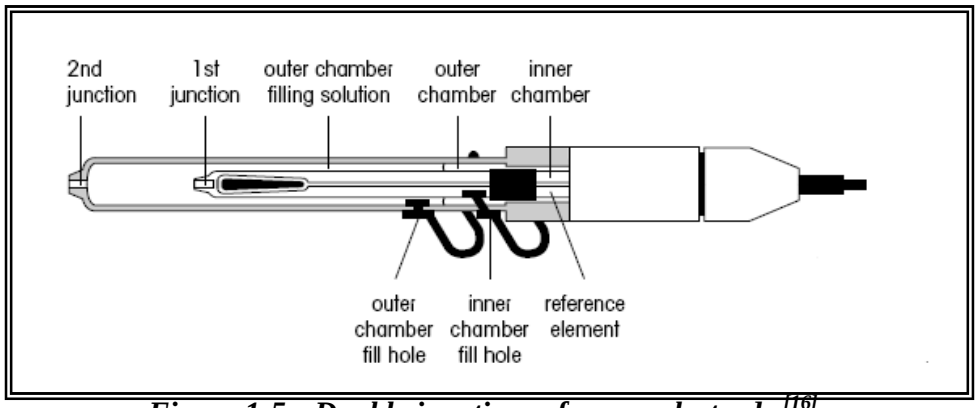


Figure 1-5:- Double junction reference electrode [16].

1-5-Characterization of ISEs:-

1-5-1-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 (or "effective concentration") of the ions in the solution[17]. This relationship is described by the Nernst equation:

E = constant ± (2.303 RT/ nF) log a **...1-5**

Figure 1-6 shows, a typical plot of the cell e.m.f (i.e. the galvanic 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.

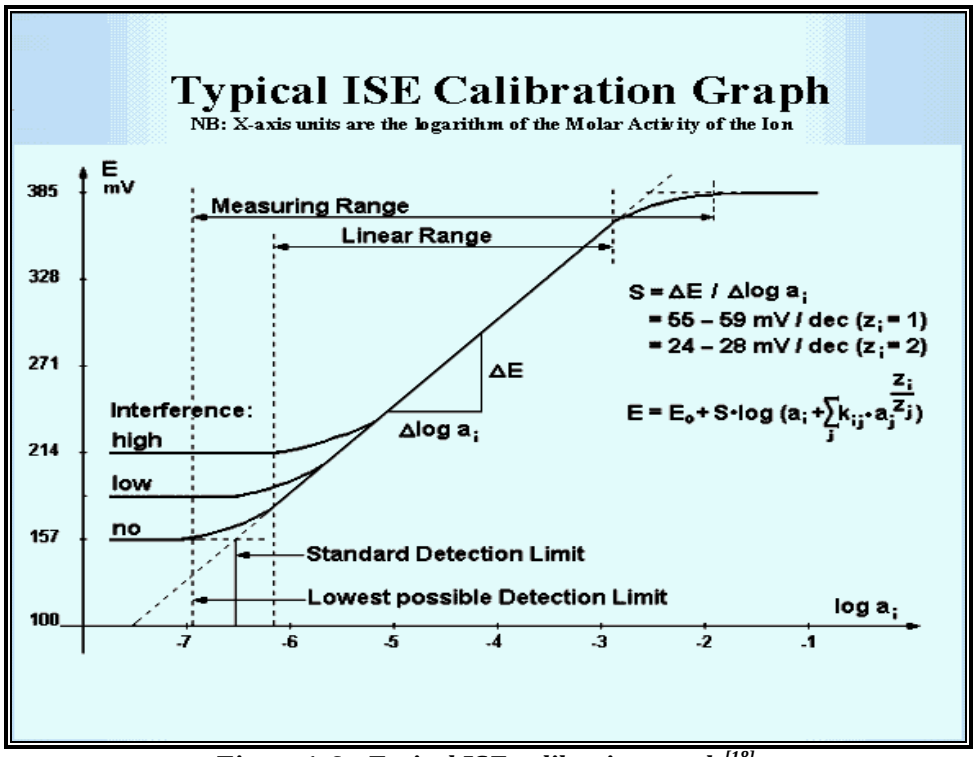


Figure 1-6:- Typical ISE calibration graph [18].

For uniformity, it is recommended that the cell e.m.f 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 abscissa (horizontal axis) with increasing activity or concentration to the right.[18] The linear rang is a part of the calibration curve through which a linear regression would demonstrate that the data

points do not deviate from linearity by more than 2 mV. For many electrodes this range can extend from 1 Molar down to 10^{-6} or even 10^{-7} Molar.

1-5-2-Slope [19, 20]:-

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. 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.

1-5-3-Detection limit:-

According to the IUPAC recommendation [19], 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. In practice, detection limit on the order of 10^{-6}-10^{-5}M is measured for most of ion selective electrodes. The observed detection limit is often governed by the presence of other interfering ions and the purity of standard solutions used for calibration curve.

1-5-4-Range of linear response:-

The linear rang 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^{-5}M and 10^{-1}M.[23]

1-5-5-Response time [24]:-

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 membrane electrode. 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 membrane, the rate of change of solution activity and the presence of interferents which all slow the response time of these electrodes.

1-5-6-Stability and lifetime:-

The stability and lifetime are features associated with the response behavior of ISEs. 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. [21, 23]

1-5-7-Selectivity [25, 26]:-

Selectivity of ion selective electrodes is quantitatively related to equilibria at the interface between the sample and the electrode membrane. Moreover, they are also required for the optimization of ionophore 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. Wrong

selectivity coefficients may be also obtained when the interfering agent is highly preferred and the electrode shows counter ion interference. A detailed recipe to determine correct potentiometric selectivity coefficients unaffected by such biases is presented. The potentiometric selectivity coefficient is expressed according to the Nicolsky-Eisenman equation as:

$$\mathbf{E = E^0 + R\,T / Z_A F \ln [a_A + \Sigma K_{A,B} (a_B)^{z_A/z_B}]} \qquad \mathbf{\ldots 1\text{-}7}$$

Where E is the measured potential; E^0 is a constant that includes the standard potential of the electrode, the reference electrode potential, and the junction potential; (z_A, z_B, a_A and a_B are the charge numbers and activities of the primary ion, A, and the interfering ion, B respectively); and $K_{A,B}$ is the potentiometric selectivity coefficient for the primary ion A against the interfering ion B. This selectivity coefficient can be determined using either separate solutions or match solutions method, containing both the analyte A, and the interfering B ions. Potentiometric selectivity coefficients can be measured with different methods that fall into two main groups:

1-5-7-1-Separate solution methods:-

1-5-7-1-1-When ($a_A = a_B$) [27]:-

The potential of a cell comprising an ion selective electrode and a reference electrode is measured with two separate solutions, one containing the ion A at the activity a_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 $K^{pot}_{A,B}$ is calculated from the equation:

$$\mathbf{\log K^{pot}_{A,B} = (E_B - E_A)\, Z_A\, F / R\,T \ln 10 + (1\text{-}z_A/z_B) \log a_A} \qquad \mathbf{\ldots 1\text{-}8}$$

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

$$\log K^{pot}_{A,B} = (E_B - E_A)/S + (1 - z_A/z_B)\log a_A \quad \text{…1-9}$$

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

1-5-7-1-2-When ($E_A = E_B$):- [27]

The potential of an ISE for the primary and interfering ions are obtained independently. Then, the activities that correspond to the same electrode potential value are used to determine the $K^{pot}_{A,B}$ value and it equal:

$$K^{pot}_{A,B} = a_A / (a_B)^{z_A/z_B} \quad \text{…1-10}$$

1-5-7-2-Mixed solution methods:-

1-5-7-2-1-Fixed interference methods (FIM) [28, 29]*:-*

The electromotive force (e.m.f) of a cell comprising an ion-selective electrode and a reference electrode (ISE cell) is measured for solutions of constant activity of the interfering ion; a_B, and varying activity of the primary ion, a_A . The e.m.f. values obtained are plotted vs. the logarithm of the activity of the primary ion as show in Figure 1-7. The intersection of the extrapolated linear portions of this plot indicates the value of a_A that is to be used to calculate $K^{pot}_{A,B}$ from the equation 1-10, where both Z_A and Z_B have the same signs, positive or negative.

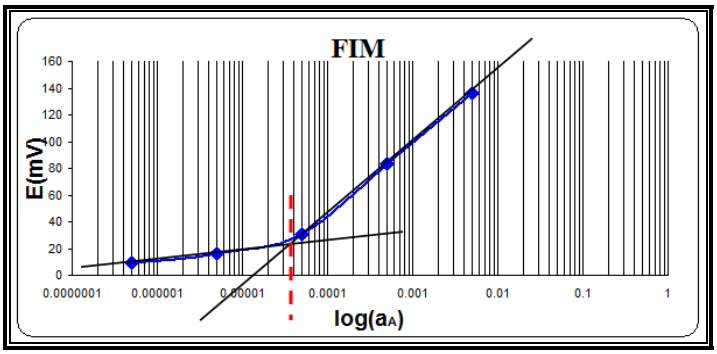


Figure 1-7:- Determination of a_A value according to FIM.

1-5-7-2-2-Fixed primary ion method (FPM) [30, 31]:-

The e.m.f of the cell comprising and a ion 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 obtained are 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 $K^{pot}_{A,B}$ from the equation 1-10.

1-5-7-2-3-Two solutions method (TSM) [30, 32]:-

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

$$K^{pot}_{A,B} = a_A \left(e^{\Delta E\, Z_A\, F / (R\, T)} - 1\right) / (a_B)^{z_A/z_B} \qquad \text{... 1-11}$$

1-5-7-2-4-Matched potential method (MPM) [33]:-

A theory is presented that describes the matched potential method (MPM) for the determination of the potentiometric selectivity coefficients $K^{pot}_{A,B}$ of ion-selective electrodes when the charge of the primary ion not equal to charge of interfering ions and used in case no possible do achieve Nernstain responses for a given interfering ion. This method is based on electrical diffuse layers on both the membrane and the aqueous side of the interface, a solution of the primary ion A with 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 Figure 1-8, another curve, I_{A+B}, is obtained from the potential change by stepwise adding the interfering ion B to the reference solution with the same composition as on curve

I_A. When the change in potential (ΔE) on curve I_A at a'_A matches that on curve I_{A+B} at a_{A+B}, the ratio between the activities of the primary ion A relative to the interfering ion B denotes the selectivity coefficient $K^{pot}_{A,B}$. The selectivity coefficient $K^{pot}_{A,B}$ is thus obtained as

$$\mathbf{K^{pot}_{A,B} = \Delta a_A / a_B} \qquad \text{... 1-12}$$

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

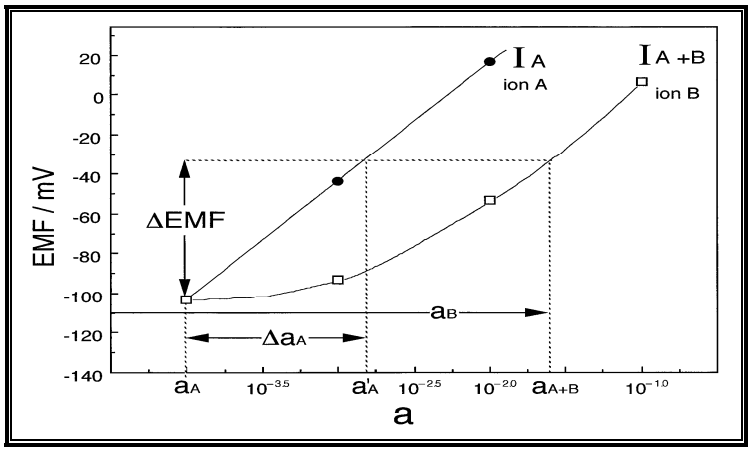


Figure 1-8:- Determination of selectivity coefficients by the matched potential method [33].

1-6-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. [20]

1-6-1-Direct potentiometry method [34]:-

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 single cycle. Each single cycle corresponds to an order of magnitude or decade, or by using

special computer graphics and calculations (eg. Microsoft Office Excel). A big advantage of this method is that it can be used to measure large batches of samples covering a wide range of concentrations very rapidly without having to change range, recalibrate or make any complicated calculations.

1-6-2-Incremental methods:-

1-6-2-1-Standard additions method (SAM) [34, 35]:-

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 found. By solving the following equation the unknown concentration can be obtained:

$$C_U = C_S / 10^{\Delta E/S} [1+ (V_U / V_S)] - (V_U / V_S) \quad \ldots 1\text{-}13$$

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. [35]

1-6-2-2-Multiple standard additions method (MSA) [36]:-

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:

$$\mathbf{E= E^0 + S\ Log\ a_A \times V_S / V_U} \qquad \textbf{...1-14}$$

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:

$$\mathbf{Antilog\ E/S = constant \times a_A V_S / V_U} \qquad \textbf{...1-15}$$

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 along abscissa yields a straight line which can be extrapolated back to an intercept on the standard volume. The concentration of sample (unknown) can be calculated:

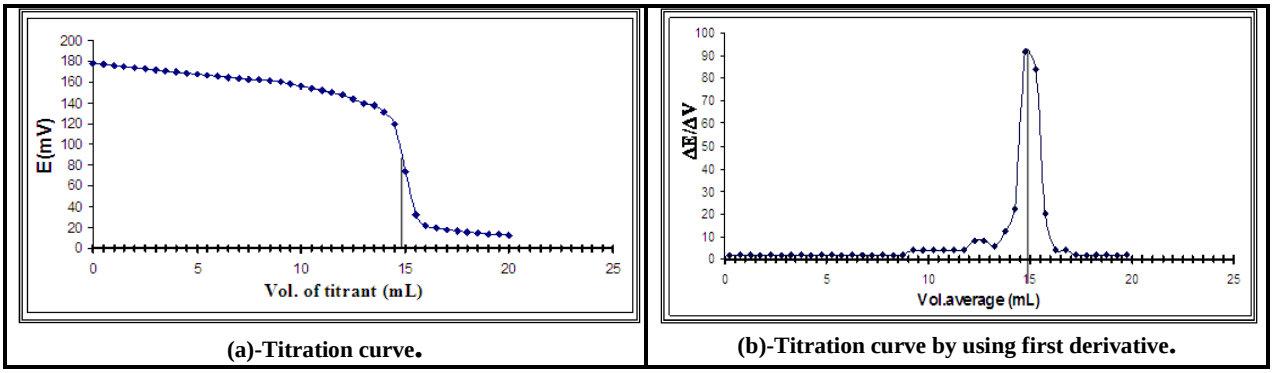
$$\mathbf{C_U = V_{so} \times C_S / V_U} \qquad \textbf{…1-16}$$

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

1-6-3-Potentiometric titration method:-

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%. Potentiometry is generally valuable as a technique for detecting the end-point of titrations where there is often a drastic

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 1-9. [37]



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

Figure 1-9:- Potentiometric titration curves by using ion-selective electrodes: (a)-titration curve, (b)-by using first derivative [38].

1-7-General applications of ISEs: - ion selective electrodes are used in a wide variety of applications for determining the concentrations of various ions in solutions. Table 1-1 shows some applications of ISEs.

Table 1-1 some applications of ISEs

Sample	Notes	Ref.
Pollution Monitoring	pH of acid rain, soil, surface water, contamination of surface water and ground water with ammonium and nitrate, contamination of waste water with cyanide, cadmium, mercury and copper, natural waters and waste matters.	39
Agriculture	Soil and fertilizer analysis for Nitrate, Ammonium and Potassium to optimize the use of fertilizer. Dissolved Oxygen and pH in ponds for fish breeding.	40
Explosives	Fluoride, chloride and nitrate have been measured in explosives and their combustion products.	41
Food Processing	Nitrate in meat and vegetables. Fluoride and calcium in milk and Cadmium in fish. Analysis of fluoride in drinking water and other drinks, corrosive effect of nitrate in canned food.	42
Biomedical Laboratories	ISEs were used to determine important species such as calcium, potassium, sodium and chloride in body fluids (blood, serum, plasma).	43

1-8-Limitation in ISE measurements:-

1-8-1-Diffusion:- Orion Research points out that differences in the rates of diffusion of ions based on size can lead to some error. In the example of sodium iodide, sodium diffuses across the junction at a given rate. Iodide moves much slower due to its larger size. To compensate for this type it is important that a positive flow of filling solution move through the junction. [20]

1-8-2-Sample ionic strength:- The total ionic strength of a sample affects the activity coefficient and that it is important that this factor stay constant. This adjustment is large, compared to the ionic strength of the sample, such that variation between samples becomes small and the potential for error is reduced.[18,20]

1-8-3- Temperature:- It is important that temperature be controlled as variation in this parameter can lead to significant measurement errors. A single degree (C) change in sample temperature can lead to measurement errors greater than 4%. [18]

1-8-4- pH:- Some samples may require conversion of the analyte to one form by adjusting the pH of the solution. Failure to adjust the pH in these instances can lead to significant measurement errors. [20]

1-8-5-Interferences:- The background matrix can effect the accuracy of measurements taken using ISE's. Covington was pointed out that some interference may be eliminated by reacting the interfering ions prior to analysis. [20]

1-9-Applications of ISEs in pharmaceutical drugs:-

The ion selective membranes are widely used for pharmaceutical analysis with advantages of determining sample directly, rapidly and simplicity. Table 1-2 shows some applications of ion selective electrodes in pharmaceuticals.

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

Pharmaceuticals	Membrane components	Liner rang (M)	Detection Limit(M)	Slope (mV/decade)	Ref.
Methacycline Hydrochloride	Methacycline-tetraphenylborate as the electroactive substance and dioctylphtalate as the plasticizing.	3×10^{-2}-6×10^{-6}	3.4×10^{-6}	52.9	44
Clozapine	Clozapine-phosphotungstate ion pair complex by use dioctyl sebacate as plasticizer.	1×10^{-5}–1×10^{-2}	3.7×10^{-6}	57.46	45
Fluconazole	Fluconazole ion pair complex by use dibutyl phthalate as plasticizer.	5×10^{-5}–5×10^{-2}	4×10^{-5}	57.0	46
Tramadol	Tramadol-tetraphenyl borate complexes by use dibutyl phosphate as plasticizer.	1×10^{-5}-1×10^{-1}	3×10^{-5}	58.06	47
Atenolol	Atenolol-phosphotungstate as an active material by used dioctyl phthalate as plasticizer.	3×10^{-4}-5×10^{-2}	5×10^{-5}	55.91	48
Acebutolol	Acebutolol-tetraphenylborate	1×10^{-3}-1×10^{-6}	6×10^{-6}	51.5	49
Tiapride	Tiapride-tetraphenylborate	1×10^{-5}-1×10^{-2}	4.3×10^{-6}	57.5	50
Amiloride	Amiloride-molybdophosphoric acid as an active material based on dibutyl phthalate as plasticizer.	1×10^{-4}-1×10^{-1}	2.5×10^{-6}	58.5	51
Dextrometho-rphan	Dextromethorphan-molybdophosphoric acid as the electro-active substance and dioctylphtalate as the plasticizing.	2×10^{-6}–1×10^{-1}	1×10^{-6}	59.5	52

Pharmaceuticals	Membrane components	Liner rang (M)	Detection Limit(M)	Slope (mV/decade)	Ref.
Nimesulide	Nimesulide - molybdophosphoric acid as the electro-active material in PVC matrix in presence of bis(2-ethyl hexyl) phthalate (BEP) as a plasticizer.	1×10^{-6}–1×10^{-2}	3.2×10^{-7}	55.6	53
Ephedrine	Reaction the Ephedrine-5-nitro-barbiturate with nitrobenzene organic solvent.	1×10^{-2}–1×10^{-5}	4.5×10^{-6}	55	54
Vitamin B_1	Ion pair with reineckate anion and use nitrobenzene as organic solvent.	1×10^{-3}–1×10^{-6}	2.5×10^{-7}	31.6	55
Naproxen	Used Tetraheptylammonium as ion pair with drug and use nitrobenzene as organic solvent.	1×10^{-1}–1×10^{-4}	1.4×10^{-4}	61	56
Cyproheptadine HCL	Prepare ion pair with tetrakis(4-chloro phenyl borate by use this plasticizer o-NPOE.	1×10^{-2}-3.5×10^{-4}	4.8×10^{-5}	58.2	57
Ibuprofen	Methyl trioctyl- ammonium chloride reacts with ibuprofen to form ion pair by use o-NPOE as plasticizer.	1×10^{-1}–1×10^{-4}	4×10^{-5}	60	58
Chlorprothixen	Prepare ion pair with sodium tetraphenylborate by use o-NPOE as plasticizer.	1×10^{-2}-6.3×10^{-4}	1.5×10^{-5}	53	59
Cetylpyridinium chloride	Prepare ion pair with Ferric thiocynate and use di-octylphthalate as plasticizer.	1×10^{-3}–1×10^{-6}	8×10^{-7}	57.5	60
Scopolamine	$(Scopolamin)_3$tungstophosphoric acid by use o-NPOE as plasticizer.	1×10^{-2}–1×10^{-6}	8×10^{-7}	54.5	61
Ampicillin	$(Ampicillin)_3$phosphotungstic acide ion pair with poly vinyl chloride.	1×10^{-1}–2.5×10^{-3}	1×10^{-4}	59	62

1-10-Promethazine hydrochloride:-

Promethazine hydrochloride, N,N-dimethyl–1–(10*H*–phenothazin–10–yl) propane-2-amine hydrochloride, $C_{17}H_{20}N_2S.HCl$, Figure 1-10, is a white or faintly yellowish crystalline powder with molecular weight of 320.9 g/mole, it melts at about (222^0C),with decomposition. It is very soluble in water; freely soluble in alcohol and in methylene chloride. [63]

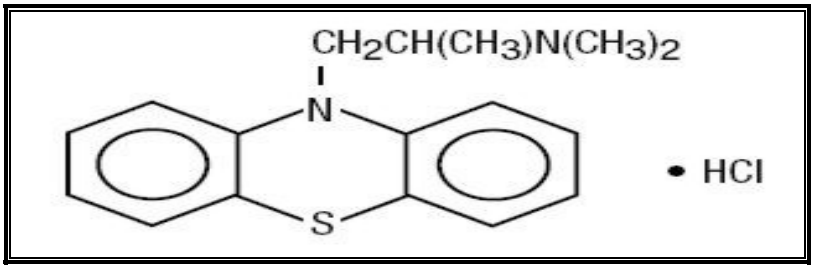


Figure 1-10:- Structure formula of promethazine hydrochloride.

Promethazine is a phenothiazine derivative that competitively blocks histamine H_1 receptors without blocking the secretion of histamine. It also is a very weak dopamine antagonist. Chemically, it's appears as a white to faint yellow crystalline powder that is practically odorless. Promethazine as the hydrochloride salt is freely soluble in water and somewhat soluble in alcohol [64]. Promethazine is commonly used to relieve itchy, irritated, and watery eyes, runny nose, sneezing and itchy skin. It is widely used as therapeutic agent for treating various mental disorders or for enhancing the analgesic, anesthetic and sedative effect. [65]

1-10-1-Analyses of promethazine hydrochloride:-

Potentiometric membrane 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 some methods for the analyses of promethazine hydrochloride.

Table 1-3:- Some methods for the analyses of promethazine hydrochloride.

Method	Notes	parameter	description	Ref.
spectrophotometry	1-Determination of promethazine in aqueous solution by oxidation of promethazine in the presence of sodium hydroxide to form an intense red soluble product.	λ =513 nm	Liner range = 4-28 µg/mL	66
	2-Promethazine forms a yellowish-green complex with platinum (IV) in hydrochloric acid.	λ =406 nm	Liner range =0.8-7.3 µg/mL	67
derivative UV-spectrophotometry	Simultaneous quantification of promethazine in the presence of sulfoxide. This method was successfully used to determine analytes in commercial promethazine pharmaceuticals.	λ =268 nm		68
Liquid chromatography	1-The chromatographic system used C18 column. The sample was analyzed using hexane: ethelacetylene, in the ratio of 3:2 v/v as a mobile phase at a flow rate of 1.0 mL/min.	Liner range=1-20x10^{-3} µg/mL		69
	2-This method is also capable of quantitatively determining three metabolites of promethazine, which uses UV-detection.	Liner range =0.1x$10^{-3\backslash}$ - 2x10^{-3} µg/mL		70

Method	Notes	parameter	description	Ref.
Liquid chromatography	3-A highly specific and sensitive method using HPLC with electrochemical detection (HPLC-ED) has been developed for the quantitative determination of promethazine in plasma.	Detection limit =0.1 µg/mL by (HPLC-ED)		71
	4-This chromatographic system used a reversed phase C18 column. The sample was analyzed using methanol: water: tryethyl amine, in the ratio of 90:10:0.1 v/v as a mobile phase at a flow rate of 1.0 mL/min.	Liner range = 0.02-0.10 µg/mL		72
	5-The chromatographic system used reversed phase C18 column. The sample was analyzed using methanol: water: octylamine in the ratio of 75:25:1 v/v as a mobile phase.	Liner range =0.001-.01 µg/mL		73
ion-selective electrode	1-Performance of promethazine electrodes based on 18-crown-6 and used DBP as plasticizer.	Slope =54.9 mV/decade	Liner range $=10^{-5}$-10^{-2}M Detection limit $=7.1 \times 10^{-6}$M	74
	2-Membrane preparation, promethazine-tetraphenylborate complex were employed as electroactive material in membrane used TBP as plasticizer.	Slope =57.8 mV/decade	Liner range $=10^{-5}$-10^{-2}M Detection limit=1×10^{-5}M	75
	3-Membrane preparation, promethazine-phosphotungstic acid complex were employed as electro-active material in membrane used DBPH as plasticizer.	Slope =56.17 mV/decade	Liner range $=5\times10^{-4}$-10^{-1} M Detection limit $=1 \times 10^{-5}$M	76

1-11-Indium:-

Indium is a soft, silver-white metallic element. Its chemical symbol is (In) atomic weight 114.43 g/mole. Indium was discovered in 1863 by the German chemists Ferdinand Reich and Heironymous Richter. It is very stable in both air and water. Indium compounds damage the heart, kidney and liver. Pure indium in metal form is considered non-toxic by most sources. In the welding and semiconductor industries, where indium exposure is relatively high, there have been no reports of any toxic side-effects. This may not be the case with indium compounds. For example, anhydrous indium trichloride ($InCl_3$) and indium phosphide (InP) are both toxic and a suspected carcinogen. One unusual property of indium that its most common isotope is slightly radioactive; it very slowly decays by beta emission to tin. This radioactivity has a half-life of 4.41×10^{14} years, four orders of magnitude larger than the age of the universe and nearly 50,000 times longer than that of natural thorium [77]. There are many types of indium compounds for example; indium (III) oxide [78], indium (III) sulfide [79], indium nitride (InN) [80].

1-11-1-Applications of indium:-

The first large scale application for indium was used in a high performance aircraft engines during World War II. Afterward, production gradually increased as new uses were found in fusible alloys and electronics. In the 1950, tiny beads of it were used for the emitters and collectors of PNP alloy junction transistors. In the middle and late 1980, the development of Indium phosphide (InP) semiconductors and Indium tin oxide thin films for liquid crystal displays (LCD) aroused much interest. [79]

1-11-1-1-Electronics:-

- Indium oxide (In_2O_3) and indium tin oxide (ITO) [81] were used as a transparent conductive coating.
- Some indium compounds such as indium sulfide and indium nitride are semiconductors with useful properties.
- Indium is used in the syntheses of the semiconductor copper indium gallium selenide, which is used for the manufacture of thin film solar cells [82].

1-11-1-2-Metal and alloys:-

- Can be plated onto metals and evaporated onto glass which forms a mirror and as good as those made with silver but has higher corrosion resistance.
- To bond gold electrical test leads to superconductors, indium is used as conducting glue.

The other use, the indium tin oxide is used as a light filter in low pressure sodium vapor lamps. The infrared radiation is reflected back into the lamp, which increases the temperature within the tube and therefore improves the performance of the lamp [83].

The first use of novel blue diode lasers to make temperature measurements based on fluorescence. As a demonstration of this principle, indium atoms were seeded as a probe species into flames and the resulting diode laser induced fluorescence allowed an accurate determination of the temperature at a point. [84]

1-11-2-Analyses of indium:-

Simple and sensitive methods used for determining indium by using spectrofluorimetric, spectrophotometric and their derivatives, high performance liquid chromatography and potentiometric analyses. Table 1-4, shows some methods for the analyses of indium.

Table 1-4:- Some methods for the analyses of indium.

Method	Notes	parameter	description	Ref.
spectrofluorimetry	Based on the formation of a fluorescent 2:1(ligand: metal) complex between indium (III) and 5-chlorosalicylidene-*o*-aminophenol at an apparent pH of 4.70 in an aqueous-ethanol medium (50% v/v ethanol) was proposed.	λ=510 nm	Liner range = 10.0–80.0 mg/L Detection limit= 1.5 mg/L	85
spectrophotometry	Based on the complex of indium (III) with benzyldodecyldimethyl ammonium bromide. Indium was determined in synthetic mixtures.	λ=514 nm	Liner range = 0.12-0.48 mg/L	86
derivative spectrophotometry	Method for rapid and selective analyses of $Ga^{3+}$and $In^{3+}$and for their simultaneous determination, by using 2-(5-bromo-2-pyridylazo)-5-diethylaminophenol in a cationic micellar medium is reported.	λ=553 nm for Ga^{3+} λ=558 nm for In^{3+}	Liner range =0.07-0.7 mg/L for Ga^{3+} 0.115-1.15 mg/L for In^{3+}	87
liquid chromatography	Determination of indium (III) as the 8-hydroxyquinoline-5-sulfonic acid derivative. Trimethyl ammonium bromide, was used as mobile phase. Response to indium is selective in the presence of other metal ions.	Liner range =0.02–0.4 mg/L Detection limit =0.1 mg/L		88
ion-selective electrode	1-Poly vinyl chloride and polyurethane matrix membrane content 5,10,15,20-tetraphenylporphrinato indium(III) ionophore plasticized with di-butylsebacate.	Slope=53 and 55mV/decade	Liner range = $4.2x10^{-6}$-$1x10^{-2}$ M and $3.3x10^{-6}$-$1x10^{-2}$M Detection limit = $2.7x10^{-6}$ and $3.1x10^{-6}$M	89
	2-The indium electrode based on 15-crown-5 (15C5) using di-octyl phenyl phosphonate (DOPP) as a plasticizer.	Slope =20.1 mV/decade	Liner range =10^{-5}-10^{-1}M Detection limit = 1.2×10^{-5}M	90

1-12-Spectrophotometric methods:-

The wavelength range of ultraviolet (UV) radiation starts from 200 nm and ends to 400 nm. The radiation of UV has sufficient energy to excite valance electrons in many atoms or molecules from their ground state to higher energy levels. The excited electrons transfer from a bonding to an anti bonding orbital. The UV radiation may be absorbed by saturated compounds that containing atoms with unshared electron pair on bonding such as nitrogen, oxygen, sulfur, halogen...etc, are capable of n-σ^* transition (150-250) nm. Most unsaturated organic compounds are based upon transitions of (n or π) electrons to π^* excited state. The visible region 400-900 sometime to near IR 1100 nm was used for all colored compounds. [91]

The wide applications of UV/Visible spectroscopy include number of inorganic metals, organic compounds, and biochemical species that absorbed ultraviolet or visible radiation and are thus amenable to direct quantitative determination. The typical applications of UV absorption spectroscopy include the determination of poly nuclear aromatic compounds such as steroids, painting materials, vitamins, drugs and there are various applications of visible spectrophotometric methods have been developed for analysis of different colored metal complexes and colored compounds. [92]

1-13-Derivative spectrophotometric methods (DS):-

The principle of operation of this technique is based on the measurement of the changes in intensity or absorbance, manually or automatically by certain instrument. The rapid progress in the technology of microcomputers has made it possible to directly present the first, second and higher order derivative spectra.

The great interest towards derivative spectrophotometry (DS) is due to the increased resolution of spectral bands, reducing the effect of spectral background interferences [93]. The DS that enhanced the resolution of overlapping spectral bands is the consequence of differentiation which discriminates against broad bands in favor of a sharp peak to an extent which increases parallel to derivative order. The main disadvantage of the derivative technique is the signal to noise ratio (SNR) becomes worse as the order of the derivative increases. A detailed study on the effect of derivatisation on the SNR has been described by O'Haver[94].The practical derivative technique includes some degree of smoothing to control the increasing in the noise. Derivative spectrophotometry (DS) is widely applied in inorganic and organic analysis, toxicology, and clinical analysis, analysis of pharmaceutical products, amino acids and proteins, in analysis of food and in environmental chemistry. In general, the application of DS is not limited to any particular case or filed, but it can be used whenever quantitative or qualitative investigations of broad spectra are difficult.

In a review published some years ago, Bosch et al. [95] have covered all the methods that were currently available to researchers for utilizing a derivative spectrophotometer and their analytical application until 1993. In recent years, the use of DS has become more practical owing to the increase in the resolving power of the analytical instrumentation and the easier access to microcomputers with appropriate software, which allow the almost instantaneous generation of the derivative spectra. Since derivative techniques have been widely applied, further development and reviews were reported. The main targets of reviews were basic characteristics of DS and a few analytical applications of DS were given. [96]

1-14-Aim of the work:-

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

The best combination of promethazine hydrochloride (ionophore), solvent mediator, and PVC matrix will be chosen. Potentiometric measurements including direct method, standard additions method and titration method will be studied. The results of normal spectrophotometric and the first-derivative (^{1}D) spectra were compared with promethazine hydrochloride electrodes results by using F-test statistics.

Several ion selective electrodes for the potentiometric determination of indium (III) were constructed by using promethazine hydrochloride, sodium tetraphenylborate (NaTPB) as additive with the same plasticizers as above. Promethazine hydrochloride and indium (III) complex were studied by spectrophotometric method.

2- Experimental part

2-1-Instruments and equipment:-

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

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

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

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

5- Combined glass electrode Orion no.91-02, (swiss made).

6- Silver-silver chloride wire.

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

8- Magnetic stirrer.

2-2-Chemicals:-

1- The chemicals compounds were used throughout the study, their molecular formula, formula weight and purity were tabulated in Table 2-1.

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

No.	Component name	Molecular formula	Formula weight	Purity	Company
1	Promethazine hydrochloride	$C_{17}H_{20}N_2S.HCl$	320.9	100%	SDI-IRAQ
2	Indium oxide	In_2O_3	277.636	99%	Fluka
3	Sodium tetraphenylborate	$C_{24}H_{20}BNa$	342.22	98%	BDH
4	Dodeca-molybdophosphoric acid	$H_3PO_4.12MoO_3.XH_2O$	1825.25	97%	BDH
5	Tetrahydrofuran	C_4H_8O	72	99.5%	Fluka
6	Polyvinyl chloride	$((CH_2\text{-}CHCl)_2)_n$	-----	99.5%	Fluka
7	Hydrochloric acid	HCl	36.45	36%	Fluka
8	Sodium hydroxide	NaOH	40.00	98%	BDH

2- Coldein tablets (5 mg promethazine hydrochloride + 450 mg paracetamol and 5 mg phenylephrine hydrochloride) made in Samara-IRAQ-SDI.

3- Other chemicals such as potassium chloride (KCl; F.W. 74.58), sodium chloride (NaCl; F.W. 58.45), calcium (II) sulfate anhydrous ($CaSO_4$; F.W. 136.0), copper (II) sulfate, anhydrous ($CuSO_4$; F.W. 159.60), manganese (11) sulfate, anhydrous ($MnSO_4$; F.W. 151), ferric (III) sulfate ($Fe_2(SO_4)_3.9H_2O$; F.W. 506.027), aluminum (III) chloride ($AlCl_3.6H_2O$; F.W. 241.50), sucrose; ($C_{12}H_{22}O_{11}$; F.W. 342.30), paracetamol; (F.W. 151.2) and gelatein; (F.W. 300.0). All chemicals and solvents were of an analytical reagent grade obtained from BDH and Fluka companies, distilled water was used throughout the study.

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

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

No.	Plasticizer's name	Molecular formula	viscosity	Purity	company
1	Di-butylphosphate (DBP)	$(C_4H_7O)_2PO(OH)$	1I2.88 CST	98.9%	Fluka
2	Di-butylphthalate (DBPH)	$C_6H_4[CO_2CH_3(CH_2)_3]_2$	14.44 CST	99%	Fluka
3	Di-octylphthalate (DOP)	$C_6H_4[CO_2C_8H_{17}]_2$	82.98 CST	98%	Fluka
4	Tri-butylphosphate (TBP)	$(C_4H_7O)_3PO$	3.114 CST	97%	Fluka
5	O-nitrophenyloctylether (ONPOE)	$O_2NC_6H_4OC_8H_{17}$	11.44 CST	98%	Fluka

2-3-Preparation of standard solutions:-

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

1- A stock solution of 0.1 M promethazine hydrochloride was prepared by dissolving 1.6045 g of pure promethazine hydrochloride in distilled water and

completing the solution up to 50 mL. The other promethazine hydrochloride standard solutions were prepared by subsequent dilution of the stock solution.

2- The stock solution of 0.1 M of indium solution was prepared by dissolving 1.3882 g of indium oxide (In_2O_3) in concentrated hydrochloric acid with heating until drying then washed it by distilled water and completing the solution up to 50 mL with distilled water. The other indium standard solutions were prepared by subsequent dilution of the stock solution ranged (10^{-1}–10^{-7}M).

3- The stock standard solution of 0.01 M molybdophosphoric acid (PM) stock standard solution prepared by dissolving 0.9126 g in distilled water and diluted up to 50 mL with distilled water.

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

5- All solutions were prepared in distilled water, stock solutions of 0.1 M of NaCl, KCl, $CaSO_4$, $CuSO_4$, $MnSO_4$, $Fe_2(SO_4)_3.9H_2O$, $AlCl_3.6H_2O$, sucrose, gelatein and paracetamol were prepared by weighted (0.2922, 0.3729, 0.680, 0.7980, 0.7550, 2.5301, 1.2075, 1.7115, 1.50 and 0.7560 g) and dissolved by distilled water in 50 mL volumetric flask. More diluted solutions were prepared by dilution from the stock solutions as required.

2-4-Preparation of ion-pair compound for promethazine hydrochloride electrodes:-

The preparation of ion-pair of (PMH-PM) was performed by mixing 50 mL of 0.01 M solution of promethazine hydrochloride (PMH) with 50 mL of 0.01 M molybdophosphoric acid with stirring. The resulting deep brown precipitate was filtered off, washed with water, dried at room temperature for two days. The

composition of the ion-pair compound (PMH-PM) was confirmed using FTIR and UV spectrum.

2-5-Preparation promethazine hydrochloride electrodes:-

Five promethazine hydrochloride ion-selective electrodes were prepared based on the use of ion-pair compound promethazine hydrochloride-molybdophosphoric acid (PMH-PM) as the electro-active substance with five plasticizers. The method of immobilization the ion-pair compounds into the PVC matrix membrane as described by Craggs et al [97]. A 0.040 g of (PMH-PM) matrix was mixed with 0.360 g of plasticizer and 0.17 g of PVC powder; all were dissolved in 5 mL of THF with stirring until a clear viscous solution was obtained.

2-6-Assembling the ion-selective electrode:-

The above solution poured into a glass casting ring about 30mm length and 35mm in diameter. It consists of two pieces; one of 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) Figure 2-1. 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 allow graduate evaporation of the solvent. The glass ring with adhering membrane was carefully removed from the glass plates as shown in Figure 2-1 (3rd step). 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 4.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 the polished end, the outer edge of the disc membrane was carefully sealed to the end of the PVC tube, step (5). Next step is connection into a glass tube, step (6). The other side of the glass tube was assembled with plastic cover in which Ag/AgCl wire was inserted

through it, the tube was filled 3/4 with 0.01 M promethazine hydrochloride solution before fixing the cover, step (7). The electrode was then conditioned by placing it in 0.1M solution containing the ion to be measured (at least 2 hour's) before using.

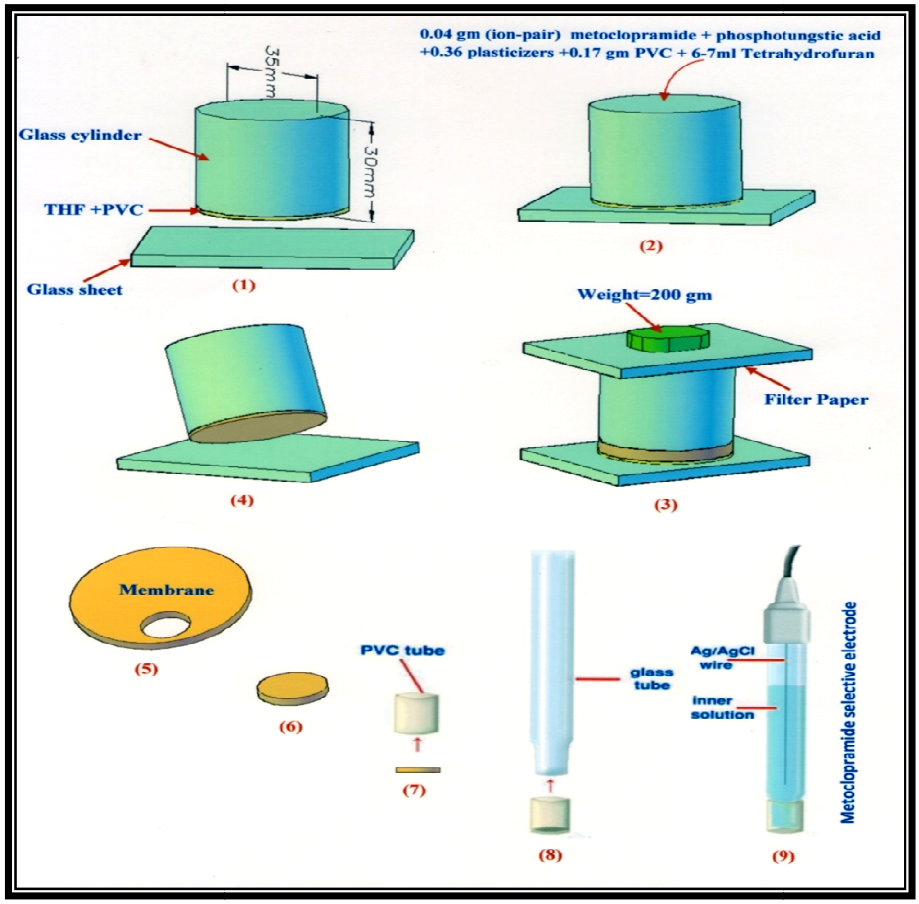


Figure 2-1:- Assembling the ion selective electrode. [98]

2-7-Preparation of indium electrodes:-

The indium ion selective electrodes were constructed using the method given by Mahajan et al [99]. A 0.040 g of promethazine hydrochloride was mixed with 0.360 g of plasticizer and 0.17 g of PVC powder and 0.040 g of sodium tetraphenylborate (NaTPB); all were dissolved in 5 mL of THF with stirring until

a clear viscous solution was obtained, then Indium electrodes prepare by the steps as shown in Figure 2-1.

2-8-Potential measurement:-

The potentiometric cell was arranged by immersing the electrode and reference electrode in 50 mL containing certain amount of analyte solutions 25 mL. The cell was equipped with a magnetic stirrer. The potential measurements were carried out at room temperature. A calibration curve was constructed for each electrode using standard analyte solutions ranged from (10^{-1}-10^{-7} M). The calibration curves were prepared by plotting the potential (E) versus log concentration by using computer program (Microsoft office Excel 2003).

From the calibration curve, the characterization parameters of an ISE were obtained, including; concentration range; slope and detection limit.

The effect of pH on the response of membrane was examined by measuring the potential of the standard solutions of concentrations (10^{-4} , 10^{-3}, 10^{-2} M) at different pH ranged from 1 to 12; obtained by addition of small volumes of hydrochloric acid and/or sodium hydroxide solutions.

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

2-9-Selectivity measurements [25, 26]:-

The influence of some inorganic ions (Na^+, K^+, Mn^{+2}, Cu^{+2}, Ca^{+2}, Fe^{+3}, Al^{+3}, paracetamol, sucrose and gelatein). For the ion selective electrodes the selectivity coefficients were determined by:-

2-9-1-The separate solution methods [27]:-

In this method, a 25 mL of $1x10^{-3}$ M solution of the prepared analyte (A) (promethazine hydrochloride or indium) and 25 mL of $1x10^{-3}$ M from each other interfering ion (B) (Na^+, K^+, Mn^{+2}, Cu^{+2}, Ca^{+2}, Fe^{+3}, Al^{+3}, paracetamol, sucrose and

gelatein) for promethazine electrodes. The interfering ion used (Na^{+}, K^{+}, Mn^{+2}, Cu^{+2}, Ca^{+2}, Fe^{+3} and Al^{+3}) for indium electrodes. The potential of each solution is measured separately. The selectivity coefficient was calculated from the equation 1-9.

2-9-2-Mixed solution methods [fixed interference method (FIM)] [28, 29]:-

In this method, a 10 mL of analyte (A) solution (promethazine hydrochloride or indium) from each 10^{-7} to 10^{-1} M are mixed with 10 mL from 0.1 M interfering ion (B) in 50 mL beaker. The potential were measured for each solution. The activities of analyte (A) are found after mixing as shown in Figure 1-7. The selectivity coefficient ($K^{pot}_{A,B}$) are calculated according to equation 1-10. The activities of interfering ion (a_B) are calculated after dilution:-

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

2-10-Sample analyses [20]:-

2-10-1-Direct method [34]:-

The potentiometry of sample is measured directly using analyte (A) solution (promethazine hydrochloride or indium) indicator electrodes. The concentration was then calculated using calibration curve of standard analyte (A).

2-10-2-Incremental methods:-

2-10-2-1-Standard additions method (SAM) [34, 35]:-

In this method, the sample of 25 mL with concentration of $1x10^{-3}$ M is introduced followed by addition of 0.5 mL of 0.01 M increment of analyte (A) solution (promethazine hydrochloride or indium). The potential were measured before and after addition. The concentration of the sample is calculated using equation 1-13 for a single point increment.

2-10-2-2-Multiple standard additions method [35, 36]:-

This method is an extension of standard additions method, the sample of 25 mL of $1x10^{-3}$ M is introduced followed by addition of 0.5 mL of 0.01 M of analyte (A) solution (promethazine hydrochloride or indium). The potential is recorded before and after each addition. The multi additions method was plotted between antilog (E/S) and the added volume of standard solution.

2-10-3-Potentiometric titration method [37]:-

2-10-3-1-Promethazine hydrochloride electrodes:-

A precipitation titration was performed for the promethazine sample under study. In this method, a 15 mL sample solution containing promethazine hydrochloride 0.01 M was titrated against 0.01 M molybdophosphoric acid (PM) solution. Potential was measured after each addition using the prepared electrode. A direct plot of potential as a function of titrant volume, the midpoint in the steeply rising portion of the curve is estimated visually and taken as end point. A second approach to end point detection is to calculate the change in potential per unit volume of titrant $\Delta E/\Delta V$ plotted versus the average volume of titrant, the maximum is the end point.

2-10-3-2-Indium electrodes:-

A precipitation titration was performed for the indium sample under study. In this method a 15 mL sample solution containing indium solution 0.01 M was titrated against 0.1 M sodium hydroxide solution [89]. Potential was measured after each addition using the prepared electrode. A direct plot of potential as a function of NaOH volume, the midpoint in the steeply rising portion of the curve is estimated visually and taken as end point. A second approach to end point detection is to calculate the change in potential per unit volume of titrant $\Delta E/\Delta V$ plotted versus the average volume titrant, the maximum is the end point.

2-11-Preparation of pharmaceutical formulation:-

Ten coldein tablets were crushed, mixed in a mortar and weighted accurately. It found that the weight of average was equal to 0.6136 g. To prepare 10^{-3} M promethazine hydrochloride, we need 0.016045 g from promethazine hydrochloride and dissolved by distilled water in 50 mL volumetric flask.

2-12-Spectrophotometric Studies:-

2-12-1-Standard solution for promethazine hydrochloride:-

Stock standard solutions of 200 mg/L drug (promethazine hydrochloride) were prepared by dissolving 0.02 g with distilled water to 100 mL, several 10 mL standard solutions ranged from 2-62 mg/L by (0.1, 0.2, 0.3, 0.4, 0.5, 1.1, 1.6, 2.1, 2.6 and 3.1) mL were prepared by dilution with distilled water.

2-12-2-pH effect:-

The best range of pH to the complex formation [PMH-In(III)] by taking 3 mL of $1x10^{-4}$ M promethazine hydrochloride and 1 mL of $1x10^{-4}$ M indium (III) solution, after that add HCl or NaOH to reach the pH range (1, 3, 5, 7, 9 and 12) and measure the absorbance at λ_{max} to find the best pH.

2-12-3-Determination ratio of ligand to metal in complex [PMH-In(III)] by continuous variation method:-

By using $1x10^{-4}$ M from promethazine hydrochloride and indium (III) solution, mixing them in acidic media with 0.2 mL of HCL as this ratio V_M:V_L (0:10, 1:9, 2:8, 3:7, 4:6, 5:5, 6:4, 7:3, 8:2, 9:1 and 10:0) then diluted to 10 mL volumetric flask with distilled water.

2-12-4-Preparation of the indium complex:-

By mixing 30 mL from $1x10^{-4}$ M of promethazine hydrochloride and 10 mL from $1x10^{-4}$ M of indium (III) solution in acidic media at pH=3.

2-12-5-FTIR absorption spectra for indium complex and promethazine hydrochloride-molybdophosphoric acid (PMH-PM) complex:-

1- Take small amount of the complex solution and dry it to 70 ^{0}C for nearly one hour. Then mixed with cesium iodide and the disk put in FTIR instrument to record the spectrum of complex.

2- Also the promethazine hydrochloride-molybdophosphoric acid (PMH-PM) complex, after precipitation the complex mixing it with potassium bromide and cesium iodide.

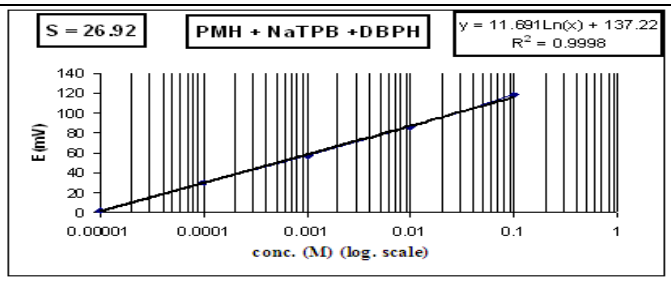
3-2-Indium (III) electrodes:-

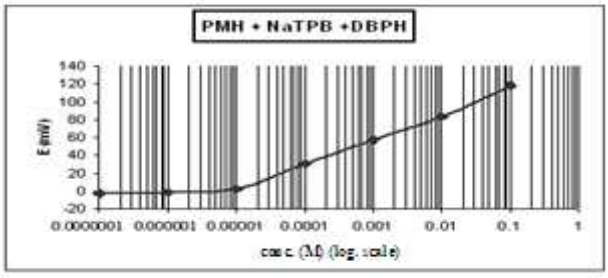
3-2-1-Sensor characteristics:-

New five indium(III) selective electrodes based on using promethazine hydrochloride (PMH) and sodium tetraphenylborate (NaTPB) as additive, used five plasticizers; Di-butyl phthalate (DBPH); Di-octyl phthalate (DOP); Di-butyl phosphate (DBP); Tri-butyl phosphate (TBP); Ortho-nitro phenyl octyl ether (ONPOE) in PVC matrix were examined. The effects of different plasticizers were studied with respect to the linear concentration range, slope, detection limit, response time and lifetime. The electrode with good characteristics was used for further studies.

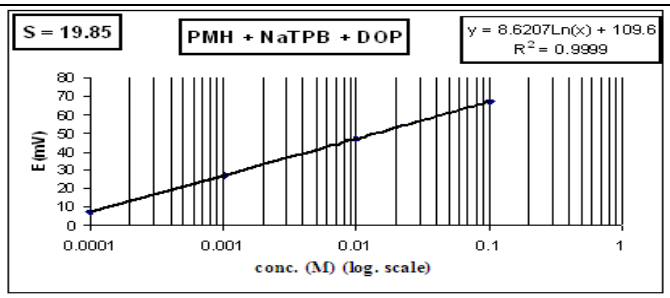
Indium (III) selective electrodes (S1, S2, S3, S4 and S5) using these plasticizers (DBPH, DOP, DBP, DBP and ONPOE) respectively, which their calibration curves shown in Figure 3-27-a, b, c, d, e respectively. These electrodes gave linear range from ($1x10^{-5}$-$1x10^{-1}$ M, $1x10^{-4}$-$1x10^{-1}$ M, $1x10^{-6}$-$1x10^{-1}$ M, $1x10^{-5}$-$1x10^{-1}$ M and $1x10^{-5}$-$1x10^{-1}$ M) and gave the slopes of (26.92, 19.85, 16.78, 12.53 and 37.25 mV/decade), with detection limit ($8x10^{-6}$ M, $8x10^{-5}$ M, $8x10^{-7}$ M, 5×10^{-6}M and $8x10^{-6}$ M) respectively.

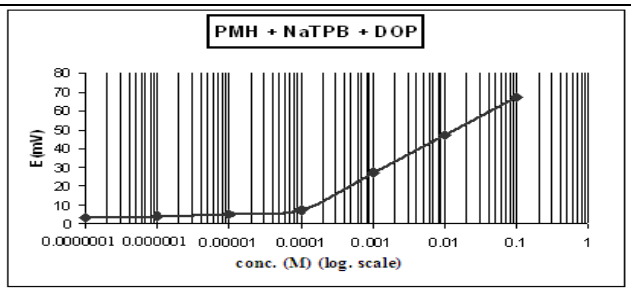
S2 electrode is the best electrode that gave the Nernst slope of 19.85mV/decade, with liner range $1x10^{-1}$–$1x10^{-4}$ M. This may be due to the compatibility between the components of the membrane, then the viscosity of DOP effect on the ion exchange between the membrane ions and the external solution ions. Consequently, DOP is more effective solvent mediator than other plasticizer due to its large dielectric constant.



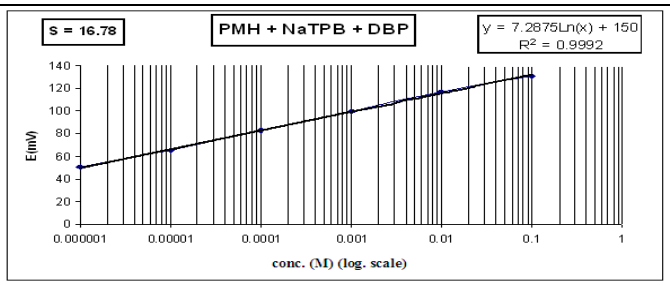


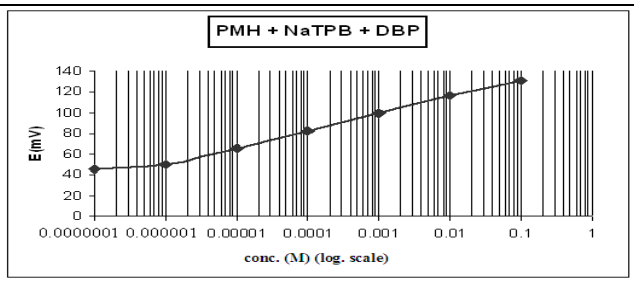
a-S1 electrode



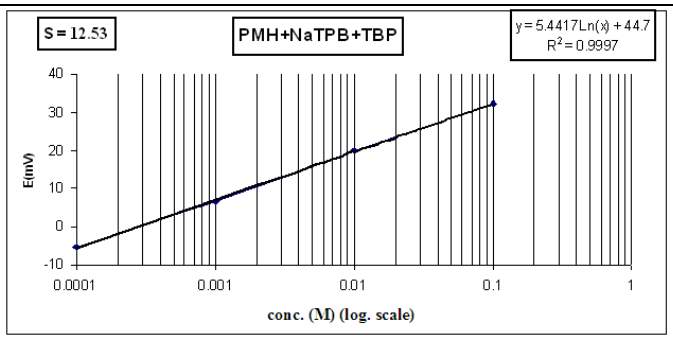


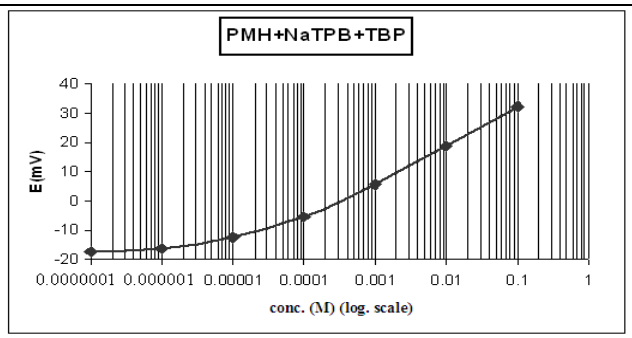
b-S2 electrode



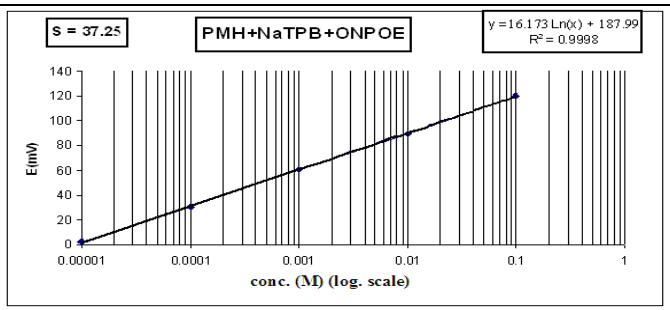


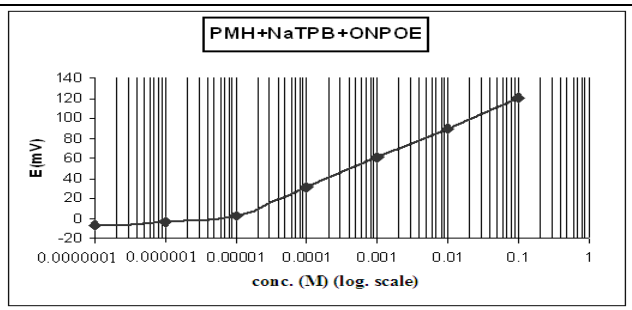
c-S3 electrode





d-S4 electrode





e-S5 electrode

Figure 3-27:-The calibration curves of indium (III) electrodes used different plasticizers: a-S1 electrode, b-S2 electrode, c-S3 electrode, d-S4 electrode, and e-S5 electrode.

S1 electrode, gave a slope of 26.92 mV/decade. This high slope may be due the viscosity of DBPH which make steric in the ion exchange between the promethazine hydrochloride ions and indium ions in the external solution. Also the effect of an additive on the performance characteristics of the membrane electrode was also investigated. The presence of mobile ion-exchange sites has also proved to be beneficial in many other respects. That mean, the additive lowers the electric membrane resistance as well as the activation barrier for the ion-exchange reaction at the membrane-solution interface. But the S4 electrode gave non-nernst slope of 12.53mV/decade. This could be due to the low viscosity of TPB (3.114 cst) which causes rapid leaching of the membrane components to the external solution. Then the low viscosity of ONPOE (11.44 cst) gave non-nernst slope, that mean homogenous membrane is formed between plasticizer and PVC.

The liner equation, slope, correlation coefficient, relative standard deviation and confidence limit (t 95%) the results are listed in Table 3-21.

Table 3-21:- The equation of calibration curves, slope, correlation coefficient, relative standard deviation of their slope and confidence limit (t 95%) for five indium (III) electrodes.

Electrode no.	Electrode membrane	Linear equation	Slope mV/Decade	slope±(ts/√N)	RSD* %	Correlation coefficient (r)
S1	**PMH+NaTPB+DBPH**	y = 11.691 Ln(x) + 137.22	26.92	26.920±0.261	0.392	0.9998
S2	**PMH+NaTPB +DOP**	y = 8.6207 Ln(x) + 109.6	19.85	19.850±0.212	0.148	0.9999
S3	**PMH+NaTPB +DBP**	y = 7.2875 Ln(x) + 150	16.78	16.780±0.103	0.249	0.9992
S4	**PMH+NaTPB +TBP**	y = 5.4417 Ln(x) + 44.7	12.53	12.530±0.163	0.526	0.9997
S5	**PMH+NaTPB +ONPOE**	y = 16.173 Ln(x) + 187.99	37.25	37.250±0.174	0.189	0.9998

t=2.78; N=5.

The response time is an important factor for all of the ion selective electrodes. The average time required for the indium (III) selective electrode to reach a potential within ±1mV of the final equilibrium value after successive immersion of a series of indium ion solutions. The dynamic response time was recorded at different concentrations of indium (III) solution. It was observed that during the long time period of 33 days. Then after 33 days, the electrode characteristics significantly drifted away from the Nernst behavior. This may be attributed to the decrease in the quantity of ionophore which means that the promethazine and the plasticizer in the membrane are migrated from the PVC membrane into the PVC tube. Table 3-22 shows the response time, detection limit, liner range and life time for these electrodes.

Table 3-22:- The liner range, detection limit, response time and lifetime for indium (III) electrodes.

Electrode no.	Electrodes membrane	Linear range (M)	Detection limit (M)	Response time (sec)			Life time (day)
				10^{-2}(M)	10^{-3}(M)	10^{-4} (M)	
S1	**PMH+NaTPB +DBPH**	1×10^{-1}– 1×10^{-5}	8×10^{-6}	20	10	8	45
S2	**PMH+NaTPB +DOP**	1×10^{-1}– 1×10^{-4}	8×10^{-5}	35	30	20	33
S3	**PMH+NaTPB +DBP**	1×10^{-1}– 1×10^{-6}	8×10^{-7}	15	10	5	30
S4	**PMH+NaTPB +TBP**	1×10^{-1}– 1×10^{-5}	5×10^{-6}	40	35	20	15
S5	**PMH+NaTPB+ONPOE**	1×10^{-1}– 1×10^{-5}	8×10^{-6}	20	10	7	21

3-2-2-Effect of pH:-

The potential remains constant over the pH range of 2.8-7.5, which may be taken as the working pH range of the sensor assembly. At pH lower than 2.8, the interference of H^+ ions is more which is due to the high rate of diffusion of H^+ ions from sample solution to membrane

matrix (extract H^+ ion) where they interact with carrier and its protonation takes place resulting in decreased selectivity of indium (III) ions. In this case, the membrane sensor responds to hydrogen ions. At pH higher than 7.5, the deviation in the electrode response occurred because of the formation of some hydroxyl complexes of indium (III) ion in solution. The pH effect studied for the tow different concentrations 10^{-3} and 10^{-2} M as shown in Figure 3-28.

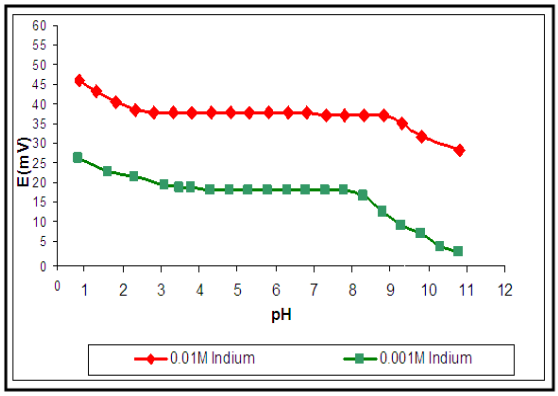


Figure 3-28:- Effect of pH on the potential of the S2 electrode, at concentrations 10^{-2} and 10^{-3} M.

Table 3-23:- Working pH ranges for S2 electrode.

Electrode no.	pH range	
S2	10^{-2}M	10^{-3}M
	2.8-8.1	2.8-7.5

3-2-3-Selectivity methods:-

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

25 mL of ($a_A = a_B = 10^{-3}$ M) two separate solutions, measured values of E_A and E_B, respectively, the value of $K^{pot}_{A,B}$ is calculated by the equation 1-9. The results of selectivity coefficients are summarized in Table 3-24.

Table3-24:- Selectivity coefficient values for S2 electrode, when E_A=29mV and the slope 19.85mV/decade.

Interfering ion	E_B (mV)	Log $K^{pot}_{A,B}$	$K^{pot}_{A,B}$
K^+	79	-3.4815	0.000329
Na^+	82	-3.3304	0.000467
Cu^{+2}	71	-3.6155	0.000242
Mn^{+2}	83	-4.2199	0.0000603
Al^{+3}	35	-0.3022	0.498
Fe^{+3}	31	-0.1007	0.793

3-2-3-2-mixed methods:-

The potential E (mV) values obtained are plotted vs. the logarithm of the activity of the indium ion (a_A) with constant activity of interfering ion (a_B =10^{-1} M). The intersection of the extrapolated linear portions of this plot indicates the value of (a_A) from Figure 3-29 to Figure 3-34 can be used to calculate $K^{pot}_{A,B}$, all results of $K^{pot}_{A,B}$ were shown in Table 3-25.

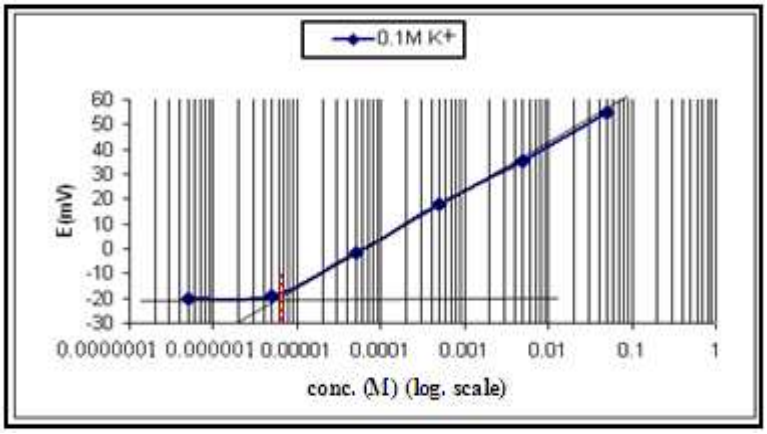


Figure 3-29:- FIM calibration curve for S2 electrode, K^+ (5×10^{-2}M) as interfering ion $a_A=7\times10^{-6}$M.

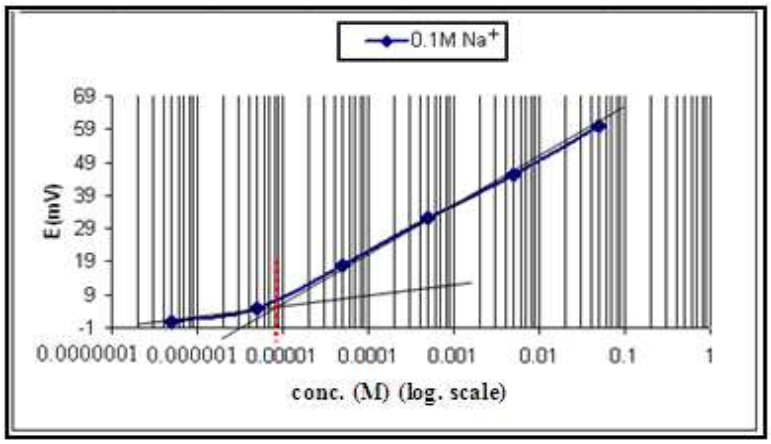


Figure 3-30:- FIM calibration curve for S2 electrode, Na^{+} (5×10^{-2}M) as interfering ion $a_A=9\times10^{-6}$M.

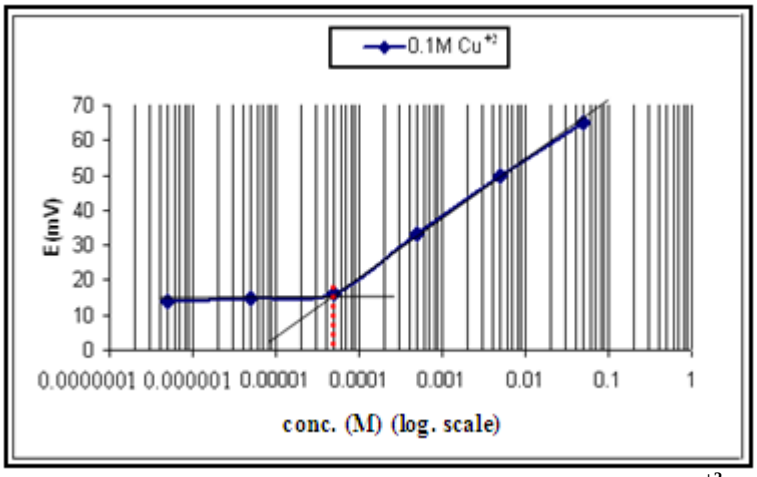


Figure 3-31:- FIM calibration curve for S2 electrode, Cu^{+2} (5×10^{-2}M) as interfering ion $a_A=5\times10^{-5}$M.

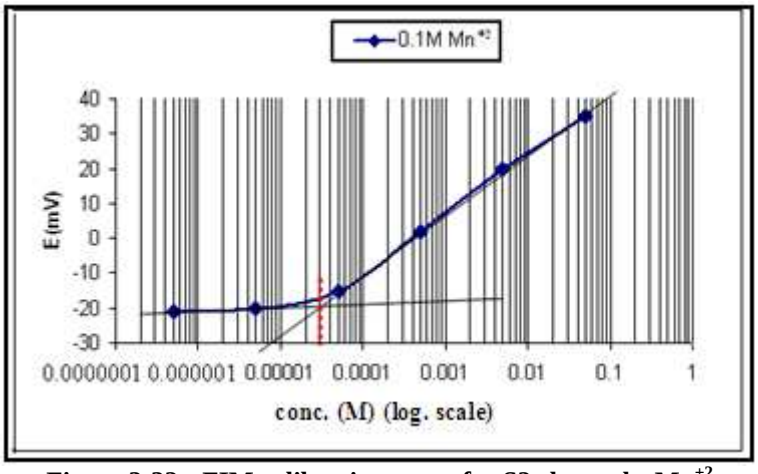


Figure 3-32:- FIM calibration curve for S2 electrode, Mn^{+2} (5×10^{-2}M) as interfering ion $a_A=3\times10^{-5}$M.

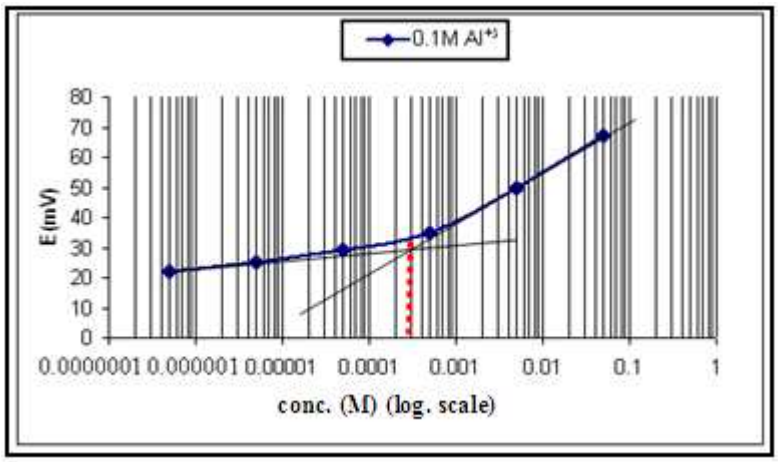


Figure 3-33:- FIM calibration curve for S2 electrode, Al^{+3} (5×10^{-2}M) as interfering ion $a_A=3\times10^{-4}$M.

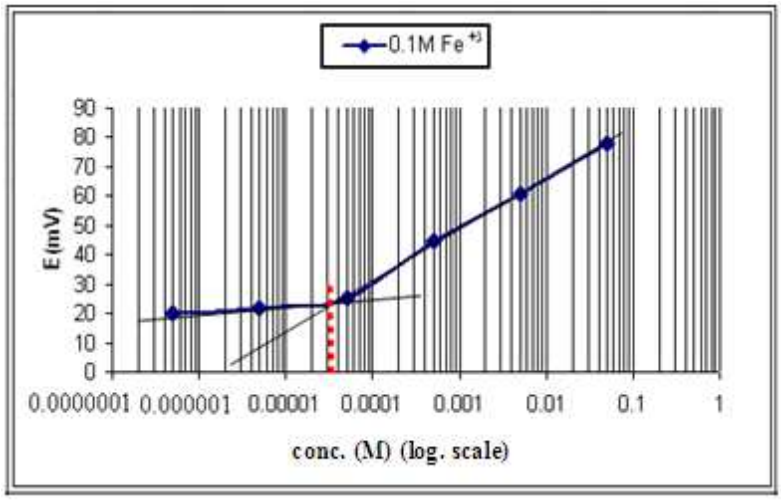


Figure 3-34:- FIM calibration curve for S2 electrode, Fe^{+3} (5×10^{-2}M) as interfering ion $a_A=3\times10^{-5}$M.

Table 3-25:- Values of $K^{pot}_{A,B}$ according to FIM , *when* $a_B = 5\times10^{-2}$ M.

Interfering-Ion	$a_B = 5\times10^{-2}$ M	
	a_A	$K^{pot}_{A,B}$
K^+	7×10^{-6}	0.056
Na^+	9×10^{-6}	0.072
Cu^{+2}	5×10^{-5}	0.000447
Mn^{+2}	3×10^{-5}	0.00268
Al^{+3}	3×10^{-4}	0.006
Fe^{+3}	3×10^{-5}	0.0006

3-2-4- Sample analyses:-

3-2-4-1- Direct method:-

The calibration curve was constructed (for S2 electrode) and the concentration of the unknown was calculated from the linear equation y = 8.6207 ln(x) +109.6 of the calibration curve which has the slope (S) ± S.D. = 19.853 ± 0.0854 and the intercept ± S.D. = 109.6 ± 0.1216, for n=5, and the results are listed in Table 3-26.

Table 3-26:- Calculation for five samples of indium (III) standard solution 10^{-4}M using direct method for S2 electrode, where slope=19.85mV/decade.

Potential reading E(mV)	The conc. of indium solution calculated from linear equation/(M)	S*	X ± (ts/√N)	Re %	E_r%	RSD%
7.81	1.005×10^{-4}	5.128×10^{-7}	$0.9994 \times 10^{-5} \pm 0.637 \times 10^{-7}$	100.5%	0.5%	0.513%
7.65	0.999×10^{-4}			99.9%	-0.1%	
7.60	0.996×10^{-4}			99.6%	-0.4%	
7.51	0.993×10^{-4}			99.3%	-0.7%	
7.80	1.004×10^{-4}			100.4 %	0.4%	

* t=2.78; N= 5.

3-2-4-2- Incremental methods:-

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

It carried out by a procedure that 0.5 mL increment of 10^{-2}M indium (III) as standard was added to 20 mL of sample as unknown. The results of calculation (SAM) for the indium (III) solution using (S2) electrode and equation 1-13, recovery, relative error and relative standard deviation for five additions of indium (III) are listed in Table 3-27.

Table 3-27:- Calculation for five additions of indium (III) standard solution using (SAM) for S2 electrode, where slope=19.85mV/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)	S*	X±(ts/√N)	Re%	E_r%	RSD%
0	29	--------	0	1	----------	7.120×10^{-6}	$0.9992\times10^{-3}\pm0.356\times10^{-3}$	----------	----------	0.713%
0.5	30.7	1.7	40	1.2196	0.999×10^{-3}			99.9%	-0.1%	
1.0	32.1	3.1	20	1.4362	0.990×10^{-3}			99%	-1%	
1.5	33.2	4.2	13.3	1.6329	0.995×10^{-3}			99.5%	-0.5%	
2.0	34.1	5.1	10	1.8139	1.004×10^{-3}			100.4%	0.4%	
2.5	34.9	5.9	8	1.9915	1.008×10^{-3}			100.8%	0.8%	

*t=2.78; N=5.

3-2-4-2-2- Multi standard additions method (MSA):-

The calibration curve for MSA for (S2) electrode was shown in Figure 3-35 by plotting antilog (E/S) versus the volume of the five additions of standard indium (III) solutions. 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 3-28.

Vol.(mL) of std. add	E(mV)	Antilog (E/S)
0	29	29.226
0.5	30.7	35.185
1	32.1	41.389
1.5	33.2	47.021
2	34.1	52.225
2.5	34.9	58.854

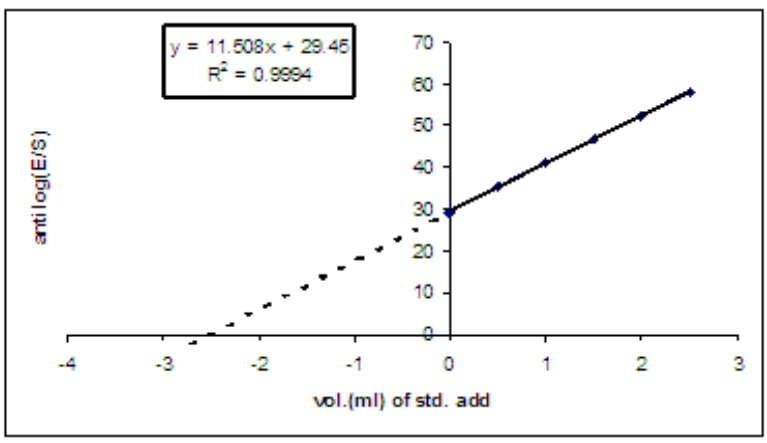


Figure 3-35:- Calibration curve of antilog (E/S) versus the volume added of standard 10^{-2}M for determination of 25 mL indium solution 10^{-3}M by (MSA).

Table 3-28:- 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=11.508x+29.45	0.9994	2.559	1.024×10^{-3}	102.4%	2.4%

3-2-4-2-3-Titration method [89]:-

The potentiometric titration for 15 mL of 0.01M of indium(III) solution with 0.1 M of sodium hydroxide (NaOH) as titrant solution as shown in Figure 3-36 and 3-37, the results of titration (Re%, E_r% and RSD%) are listed in Table 3-29.

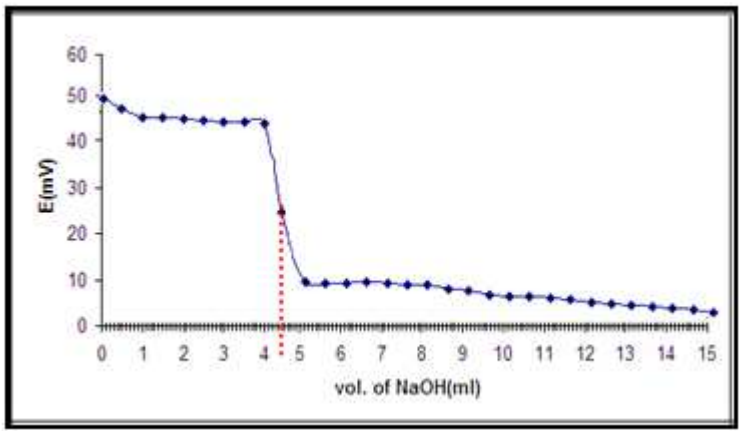


Figure 3-36:- Titration curve of S2 electrode, for 15 mL of 0.01M of indium solution with 0.1 M of sodium hydroxide as a titrant solution.

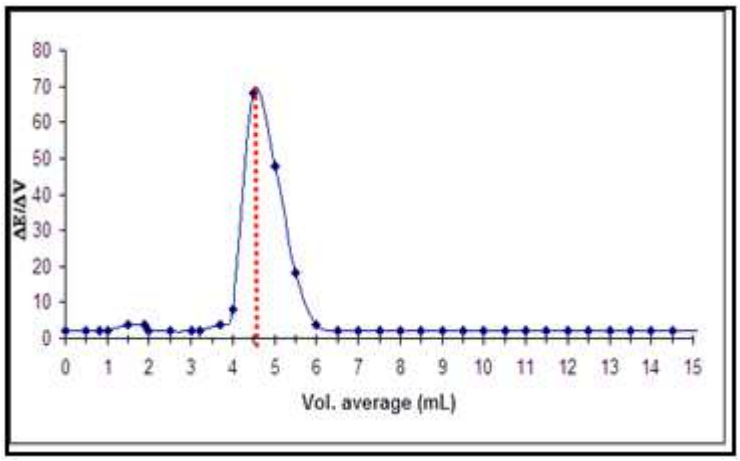


Figure 3-37:- Titration curve of S2 electrode, by using first derivative.

Table 3-29:- Standard indium solution analyses results by using titration method for S2 electrode.

Titration Figure	Vol. mL at the end point	C_U(M)	Re%	RSD*%
Figure 3-36	4.5	1.00×10^{-2}	100 %	0.141%
Figure 3-37	4.6	1.002×10^{-2}	100.2%	

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

3-2-5-UV-Spectrophotometry:-

3-2-5-1-The spectrum of indium complex [PMH-In(III)]:-

Figure 3-38, show the absorption spectra of purple drug complex of promethazine hydrochloride and indium (III) solution, shows two absorption wavelengths 353 and 258 nm. The complex solution containing of 30 mL of 10^{-4} M of promethazine hydrochloride and 10 mL of 10^{-4} M of indium (III) solution, complex formation in the acidic media at pH=3.

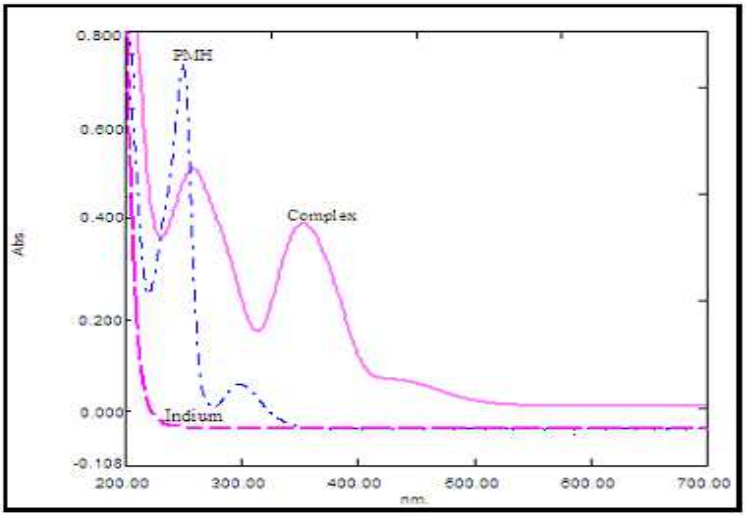


Figure 3-38:- Spectrum of complex solution PMH (30 mL) + In(III) (10 mL) in pH=3.

3-2-5-2-The Effect of pH on [PMH-In(III)] complex spectrum:-

The spectra for series of solutions containing 10 mL of 10^{-4} M of indium (III) solution and 30 mL of 10^{-4} M promethazine hydrochloride with different pH ranged from 1 to12 using HCl and NaOH. In the acidic

addition, get the optimize pH in the pH=3 and the absorbance equal 0.447 for wavelength at 258 nm and 0.347 for 353 nm. The wavelengths and absorbance are listed in Table 3-30. The spectrums of these additions are shown in Figure 3-39.

Figure 3-40, show the pH effect on the absorbance of complex at different pH at λ 258 nm.

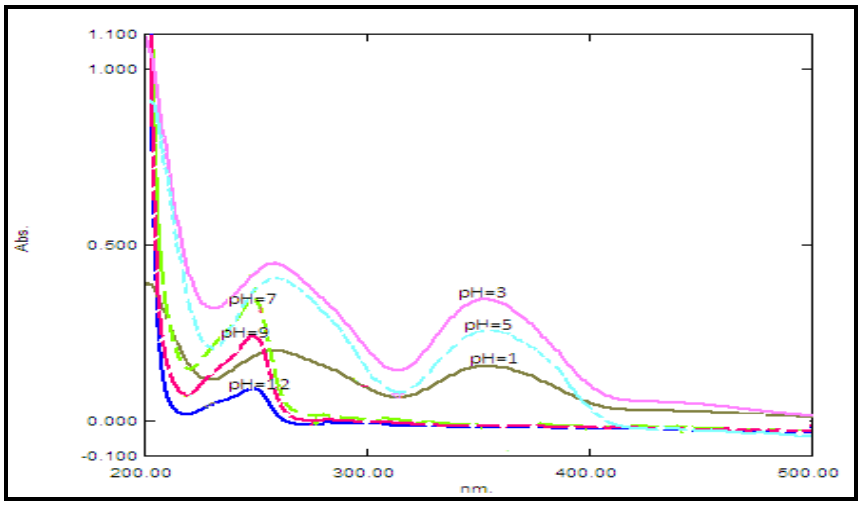


Figure 3-39: Spectrum of complex solution at different pH.

Table 3-30:- The values of absorbance and wavelength of spectrum complex at different pH.

pH=1		pH=3		pH=5		pH=7		pH=9		pH=12	
Λ nm	abs.	λ nm	abs.	λ nm	abs.	λ nm	abs.	λ nm	abs.	λ nm	abs.
258	0.200	258	0.447	258	0.416	249	0.345	249	0.241	249	0.09
353	0.155	353	0.347	353	0.252	……	……	……	……	…….	……

Figure 3-40:- Effect of pH on the absorbance for complex [PMH-In(III)] at λmax=258 nm.

3-2-5-3-Determination of ligand to metal ratio in complex [PMH-In(III)] by continuous variation method (Job method):-

Figure 3-41, shows the continuous variation method between promethazine hydrochloride and indium (III) solution ion, and the ratio $V_L:V_M=3:1$.

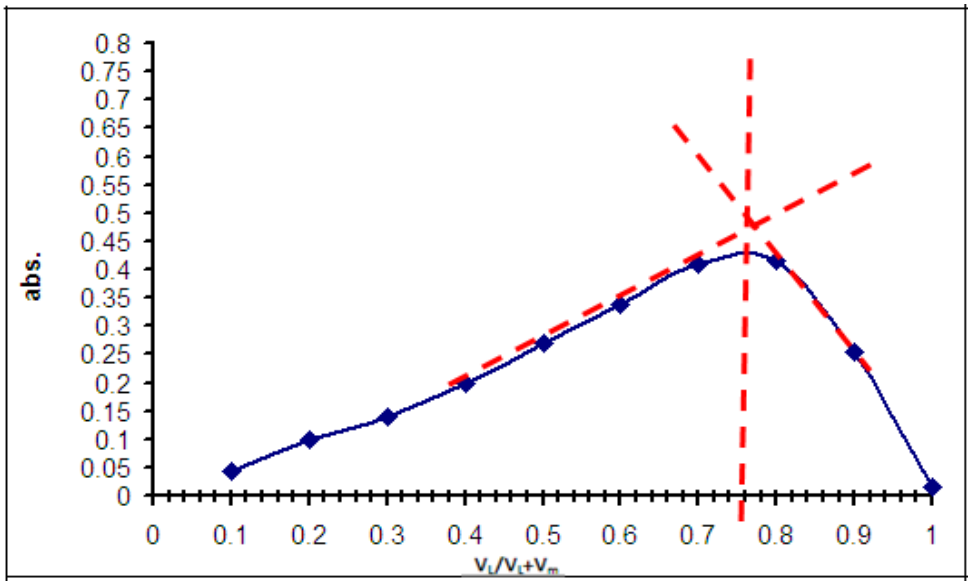


Figure 3-41:- Continuous variation method for complex [PMH-In(III)].

3-2-5-4-The FTIR spectra for indium complex [PMH-In(III)]:-

The complex characterized is obtained by it is FTIR spectra as shown in (Figure 3-42-(a) in CsI for promethazine hydrochloride alone and Figure 3-42-(b) in CsI for indium (III) complex [PMH-In(III)]). The characterized of indium (III) complex [PMH-In(III)] is deep purple precipitate. The FTIR spectra indicate and improved the formation of the indium (III) complex [PMH-In(III)]. The functional groups for both promethazine hydrochloride and the complex are listed in Table 3-31.

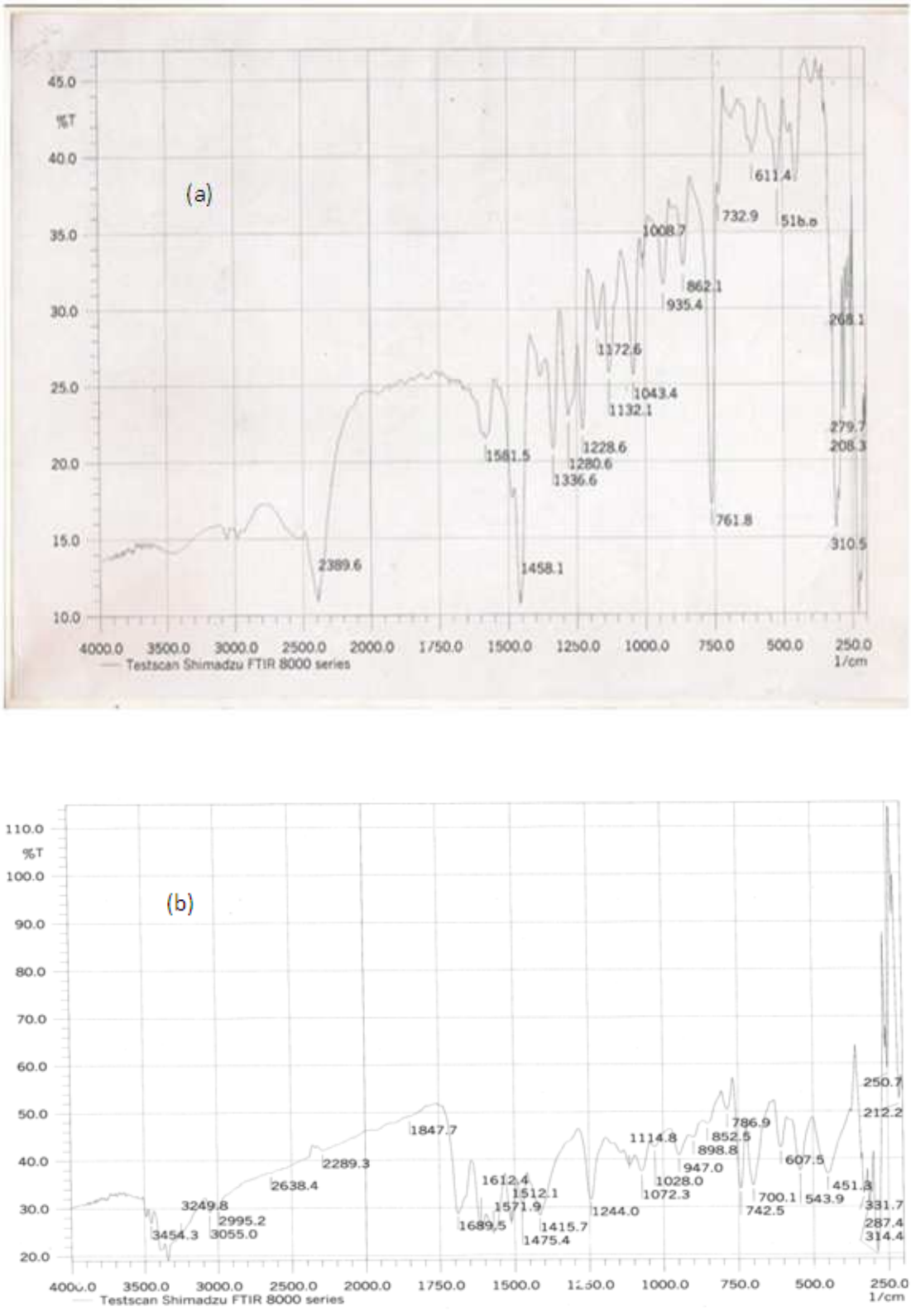


Figure 3-42: FTIR spectra (a)-promethazine hydrochloride and (b)-complex [PMH-In(III)]by using CsI.

Table 3-31:- The functional groups obtained from the spectrum for each promethazine hydrochloride and complex [PMH-In(III)].

Functional groups	Promethazine hydrochloride(PMH) cm^{-1}	Complex [PMH-In(III)] cm^{-1}
ν (R_3NH^+) Cl^-	2389	-
ν (C=C) aromatic	1581	1571
ν (C-H) bend	1458	1475
ν ($N(CH_3)_2$	1228	1244
ν (C-N)	1132	1114
Ortho disub. Benzene	1043	1028
ν (C-S-C)	761	742
ν (M-L)	-	451

3-3- Conclusions:-

The two kinds of electrodes were prepared in this study based on PVC matrix for promethazine hydrochloride and indium(III).

1- Ion selective electrode for promethazine hydrochloride:

ISE method included fabrication of membranes for promethazine hydrochloride was constructed by molybdophosphoric acid with drug as ion-exchanger and many plasticizers: Di-butyl phthalate (DBPH), Di-octyl phthalate (DOP), Di-butyl phosphate (DBP), Tri-butyl phosphate (TBP), Ortho-nitro phenyl octyl ether (ONPOE) in PVC matrix membrane. The best electrode for promethazine hydrochloride was (E1) electrode which used to determine promethazine hydrochloride in the pharmaceutical sample (coldein tablets). Also there is no interference for some interfering ion (Na^+, K^+, Mn^{+2}, Cu^{+2}, Ca^{+2}, Fe^{+3}, Al^{+3}, paracetmol, sucrose and gelatein), it also has the working pH in the range (2.3–7.8). The practical utility of the electrode has been demonstrated by use it as

indicator electrode in potentiometric precipitation titration of promethazine hydrochloride solution with molybdophosphoric acid solution. Direct method, standard additions method and multi standard additions method have been also successfully applied and showing a very good results. The results of these analytical methods were showed to be simple, rapid and with a good agreement in term of precision with direct method of ion selective electrode of the studied analytes by using F-test at 95% confidence interval.

2- Ion selective electrode for indium (III):

ISE method included fabrication of membranes for indium(III) based on using promethazine hydrochloride (PMH) and sodium tetraphenylborate (NaTPB) as additive, used five plasticizers; Di-butyl phthalate (DBPH); Di-octyl phthalate (DOP); Di-butyl phosphate (DBP); Tri-butyl phosphate (TBP); Ortho-nitro phenyl octyl ether (ONPOE) in PVC matrix were examined. Also there is no interference for some interfering ion (Na^{+}, K^{+}, Mn^{+2}, Cu^{+2}, Ca^{+2}, Fe^{+3} and Al^{+3}), it also has the working pH in the range (2.8-7.5). The practical utility of the electrode has been demonstrated by use it as indicator electrode in potentiometric precipitation titration of indium (III) solution with sodium hydroxide solution. The complex of promethazine hydrochloride and indium (III) was studied by UV-spectrophotometric method and determination the promethazine hydrochloride to indium (III) ratio (3:1) by using Job method.

3-4-Future Work:-

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

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

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

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

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

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

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

7- Study the selectivity behavior using other methods and also by using more interfering ions.

3-Results and Discussion

3-1-Promethazine electrodes:-

3-1-1-The FTIR spectra for promethazine and promethazine-molybdophosphoric acid (PMH-PM):-

The complex is obtained by conversion promethazine hydrochloride to promethazine hydrochloride-molybdophosphoric acid (PMH-PM) which characterized by their FTIR spectra as shown in (Figure 3-1-(a) in KBr and Figure 3-2-(a) in CsI) for promethazine hydrochloride alone, (Figure 3-1-(b) in KBr and Figure 3-2-(b) in CsI) for promethazine hydrochloride-molybdophosphoric acid (PMH-PM) deep brown precipitate. The FTIR spectra indicate and improve the formation of the complex PMH-PM. The functional groups for both promethazine hydrochloride and the complex are listed in Table 3-1.

Table 3-1:- The functional groups obtained from the spectrum for each promethazine hydrochloride and promethazine hydrochloride-molybdophosphoric acid.

Functional group	Promethazine hydrochloride(PMH) cm^{-1}	Complex (PMH-PM) cm^{-1}
ν (C-H) aliphatic	2927	2858
ν (R_3NH^+) Cl^-	2368	-
ν (C=C) aromatic	1568	1554
ν (C-H) bend	1452	1460
ν ($N(CH_3)_2$	1222.8	1213
ν (C-N)	1122	-
Ortho disub. Benzene	1037	1062
ν (C-S-C)	758	794
ν (M-N)	-	474

Figure 3-1:- FTIR spectra (a)-promethazine hydrochloride and (b)-(PMH-PM) complex by using KBr.

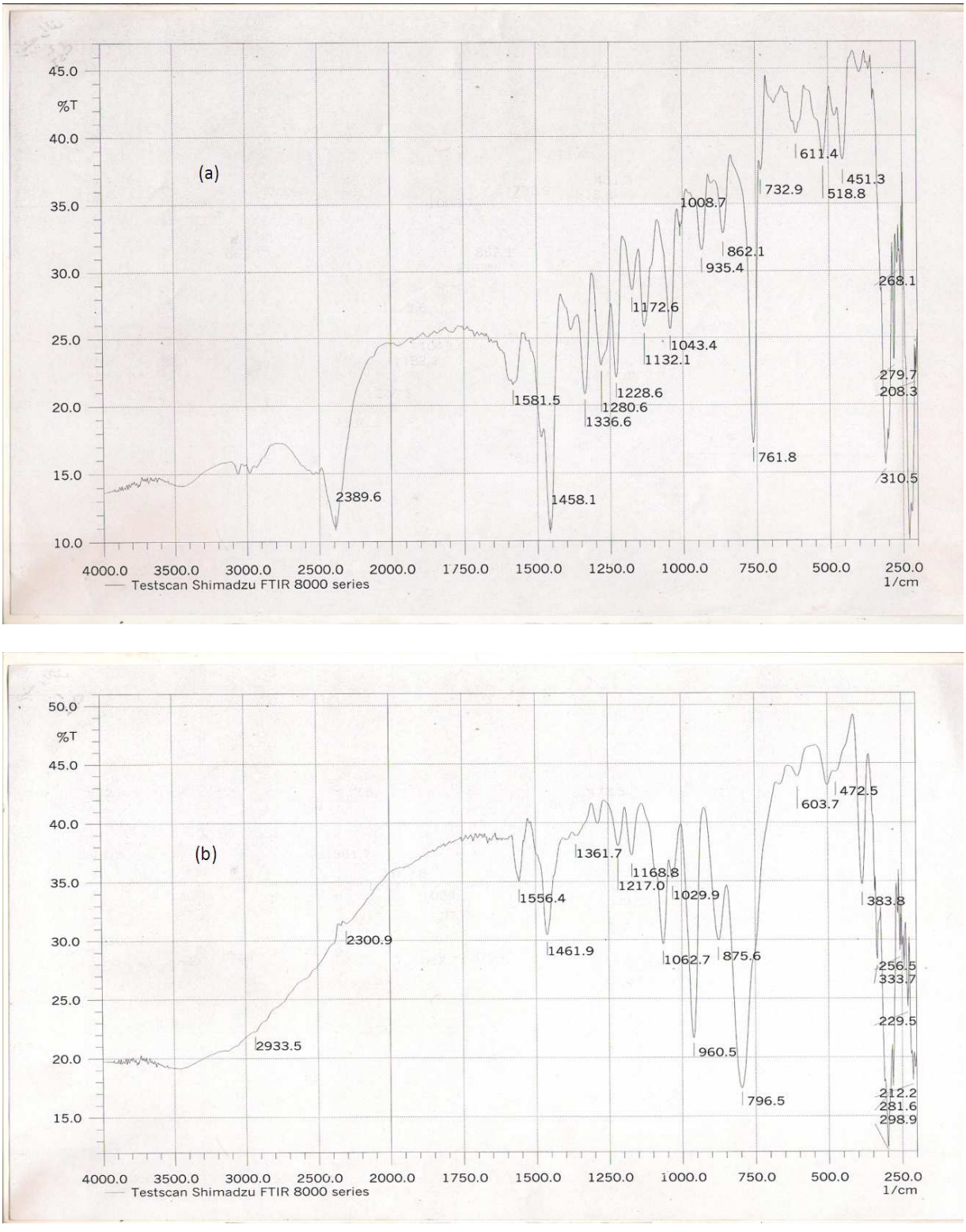


Figure 3-2:- FTIR spectra (a)-promethazine hydrochloride and (b)-(PMH-PM) complex by using CsI.

3-1-2-Sensor Characteristics:-

Five electrodes of promethazine hydrochloride based on promethazine hydrochloride-molybdophosphoric acid (PMH-PM) ion-pair complex as the electro-active material and five plasticizers such as: Di-butyl phthalate (DBPH); Di-octyl phthalate (DOP); Di-butyl phosphate (DBP); Tri-butyl phosphate (TBP); Ortho-nitro phenyl octyl ether (ONPOE) in PVC matrix were examined. The effects of different plasticizers were studied with respect to the linear concentration range, slope, detection limit, response time and lifetime. The potential values of these electrodes were plotted versus the logarithm of concentration of drug. All membranes were soaked in $1x10^{-1}$ M drug solution for one hour for condition by the membrane.

Promethazine hydrochloride electrodes (E1, E2, E3, E4 and E5) using these plasticizers (DBPH, DOP, DBP, TBP and ONPOE) respectively, which their calibration curves shown in Figure 3-3-(a, b, c, d, e) respectively. These electrodes gave the linear range from ($1x10^{-5}$-$1x10^{-1}$, $1x10^{-4}$-$1x10^{-1}$, $1x10^{-5}$-$1x10^{-1}$, $5x10^{-4}$-$1x10^{-1}$ and $1x10^{-4}$-$1x10^{-1}$ M) and gave the slopes of (57.27, 54.08, 49.79, 46.76 and 44.52 mV/decade), with detection limit ($8x10^{-6}$ M, $6x10^{-5}$ M, $6x10^{-6}$ M, 8×10^{-5}M and $8x10^{-5}$ M) respectively. The results were summarized in Table 3-2.

The E1 electrode, is the best electrode which gives the Nernst slope 57.27mV/decade and correlation coefficient 0.9999, the slope value because the high mixing between the (DBPH) and the poly phenyl chloride (PVC) due to the compatibility of the plasticizer used to the electro-active compound in both structure and composition.

Table 3-2:- The parameters of five promethazine hydrochloride electrodes.

Electrode no.	Electrode membrane	Slope (mV/Decade)	Linear concentration range (M)	Detection limit (M)	Response time (sec)			Lifetime (day)
					10^{-2} (M)	10^{-3} (M)	10^{-4}(M)	
E1	**PMH-PM+DBPH**	57.27	1×10^{-5}– 1×10^{-1}	8×10^{-6}	8	12	25	62
E2	**PMH-PM +DOP**	54.08	1×10^{-4}–1 $\times10^{-1}$	6×10^{-5}	5	10	30	22
E3	**PMH-PM+DBP**	49.79	1×10^{-5} –1× 10^{-1}	6×10^{-6}	12	20	35	35
E4	**PMH-PM+TBP**	46.76	5×10^{-4}– 1×10^{-1}	8×10^{-5}	7	15	20	19
E5	**PMH-PM+ONPOE**	44.52	1×10^{-4}– 1×10^{-1}	8×10^{-5}	6	12	30	7

From the results obtained, the E1 electrode was considered to be more sensitive than the other electrodes because of a higher slope value compared with slope value than the other electrodes. The E4 electrode gave non-Nernst slope, this could be due to the low viscosity of TPB (3.114 cst) which causes rapid leaching of the complex out of the membrane when it is in contact with aqueous solution. Also the low viscosity of ONPOE (11.44 cst) gave non-Nernst slope of 44.52 mV/decade. Then the E2 electrode gave slope 54.08 mV/decade, due to the viscosity of the DOP (82.98 cst) increase the ion-exchange between ion-pair of complex (PMH-PM) in membrane and the external solution.

E3 electrode, gave slope of 49.79 mV/decade due to the viscosity of the plasticizers; for example, the high viscosity of the DBP (112.88 cst) plasticizer which decrease the ion-exchange process between ion-pair complex (PMH-PM) in membrane and the external solution of promethazine.

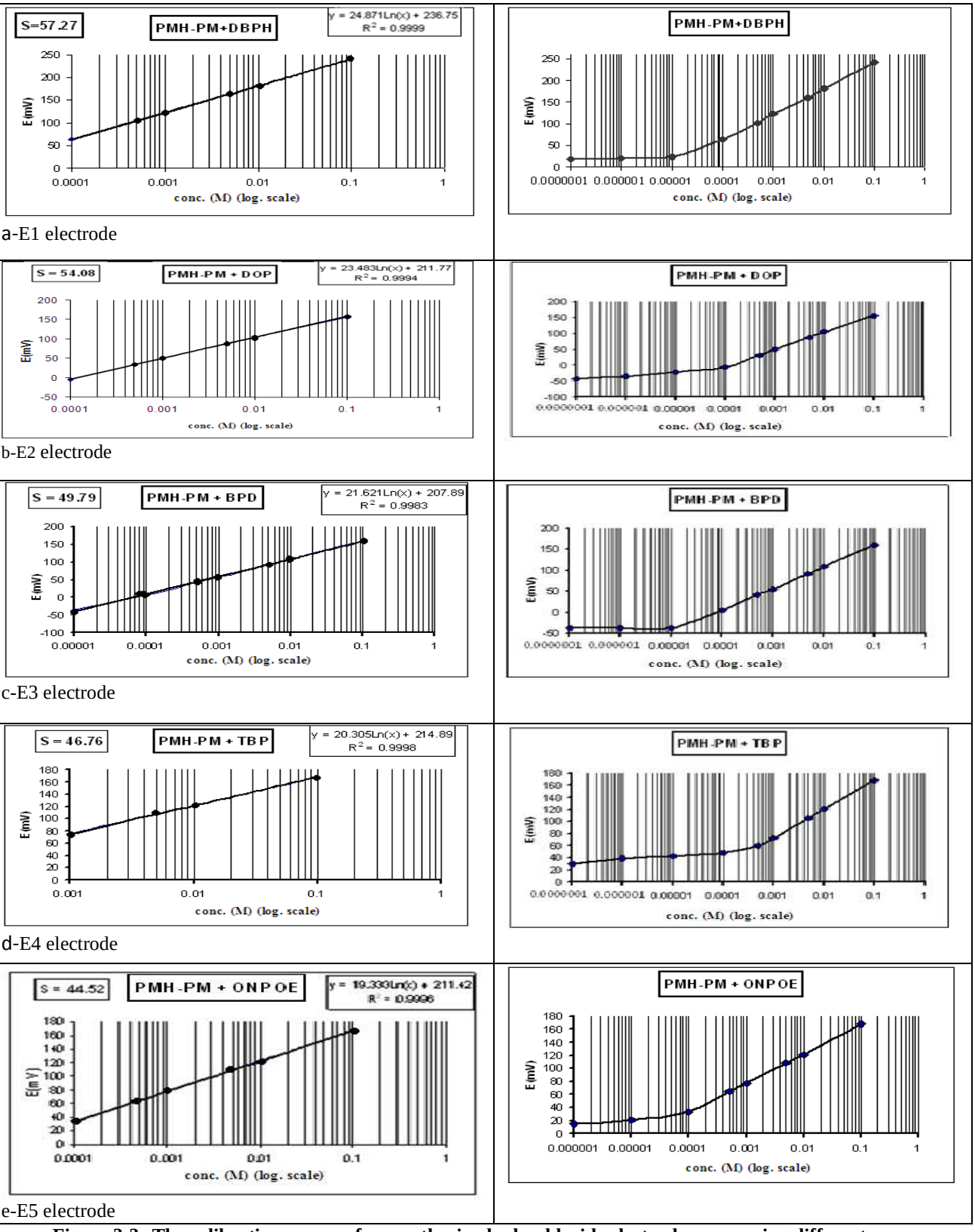


Figure 3-3:-The calibration curves of promethazine hydrochloride electrodes were using different plasticizers: a-E1 electrode, b-E2 electrode, c-E3 electrode, d-E4 electrode, and e-E5 electrode.

The working rang characteristics for promethazine hydrochloride sensors the investigated electrodes were assessed on the basis of the calibration curves which were obtained by measuring of the potential values of the set of promethazine hydrochloride solutions ranged (10^{-1}–10^{-7}M). The parameters of five promethazine hydrochloride electrodes, equations of the linear range, slopes, correlation coefficients, relative standard deviation and confidence limit (t 95%) are listed in Table 3-3.

Table 3-3:- The equation of calibration curves, slopes, correlation coefficients, relative standard deviation and confidence limit (t 95%) for five promethazine hydrochloride electrodes.

Electrode no.	Electrode membrane	Linear equation	Slope (mV/decade)	slope±(ts/√N)	RSD* %	Correlation coefficient (r)
E1	**PMH-PM+DBPH**	y = 24.871 Ln(x) + 236.75	57.27	57. 270±0.225	0.159	0.9999
E2	**PMH-PM +DOP**	y = 23.483 Ln(x) + 211.77	54.08	54.080±0.249	0.358	0.9997
E3	**PMH-PM +DBP**	y = 21.621 Ln(x) + 207.89	49.79	49.790±0.603	0.674	0.9991
E4	**PMH-PM +TBP**	y = 20.305 Ln(x) +214.89	46.76	46.760±0.871	0.708	0.9999
E5	**PMH-PM+ONPOE**	y = 19.333 Ln(x) + 211.42	44.52	44520±0.626	0.743	0.9998

*** The result of three times repeated;** t= **4.3; N= 3.**

3-1-3-Effect of pH:-

The effect of pH on the electrode potentials for promethazine hydrochloride selective membrane was examined by measuring the potential for the three different promethazine hydrochloride concentrations 10^{-4}, 10^{-3} and 10^{-2} M. The obtained responses of electrodes were remained constant at pH range from 2 to 8 and then decrease when the pH increase. This may be attributed to the low solubility of promethazine hydrochloride in the alkali solution.

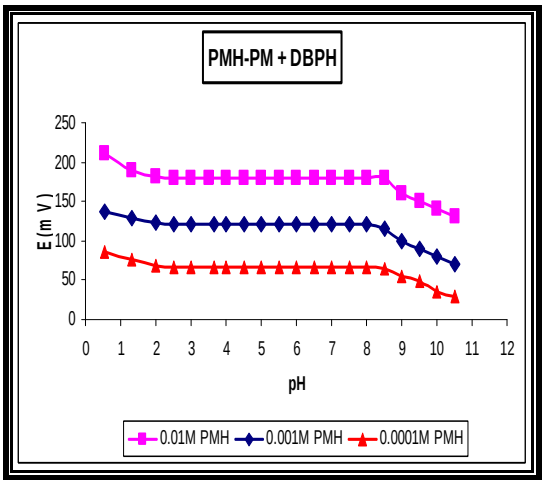


Figure 3-4:- Effect of pH on the potential of the E1 electrode at concentrations 10^{-2}, 10^{-3} and 10^{-4} M.

Table 3-4:- Working pH ranges for promethazine hydrochloride E1 electrode.

Electrode no.	pH range		
E1 electrode	10^{-2}M	10^{-3}M	10^{-4}M
	2.1 – 8.1	2.3 – 7.8	1.9 – 8.3

3-1-4-Selectivity methods:-

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

In the first case when ($a_A = a_B = 10^{-3}$ M) The potential is measured with two separate solutions, one containing the promethazine hydrochloride 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 3-5.

Table3-5:- Selectivity coefficient values for E1 electrode, when E_A=123 mV and the slope 57.27 mV/decade.

Interfering Ion	E_B (mV) of 10^{-3} M	*Log* $K^{pot}_{A,B}$	$K^{pot}_{A,B}$
K^+	-20.3	-2.5022	0.00315
Na^+	-14.1	-2.3939	0.00403
Cu^{+2}	-6.9	-3.7682	0.000171
Mn^{+2}	-19.1	-3.9812	0.000104
Ca^{+2}	-5.2	-3.7385	0.000183
Al^{+3}	31.1	-3.6147	0.000243
Fe^{+3}	-12.3	-4.3724	0.0000424
paracetamol	5.8	-2.0464	0.00898
sucrose	4.9	-2.0622	0.00866
gelatein	-1.2	-2.1686	0.00678

From the Table 3-5, all values of $K^{pot}_{A,B}$ are less than (0.1), This reflects a very high selectivity of this electrodes towards promethazine hydrochloride.

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

The potential of cell is measured for the solutions at constant concentration of the interfering ion (a_B) at first used 1×10^{-1} M that calculated in 20 mL total volume after mixed it with varying concentration of the promethazine hydrochloride (a_A). The potential values obtained are plotted vs. the logarithm of the concentration of the promethazine hydrochloride. The intersection of the extrapolated linear portions of this plot determination the value of (a_A).

from Figure 3-5 to Figure 3-14 can be used to calculate $K^{pot}_{A,B}$, all results of $K^{pot}_{A,B}$ were listed in Table 3-6.

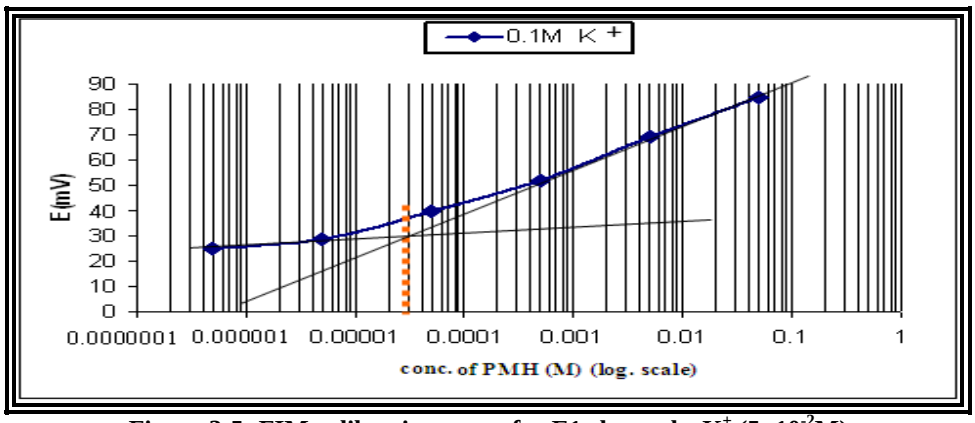


Figure 3-5: FIM calibration curve for E1 electrode, K^+ (5×10^{-2}M) as interfering ion $a_A = 3\times10^{-5}$M.

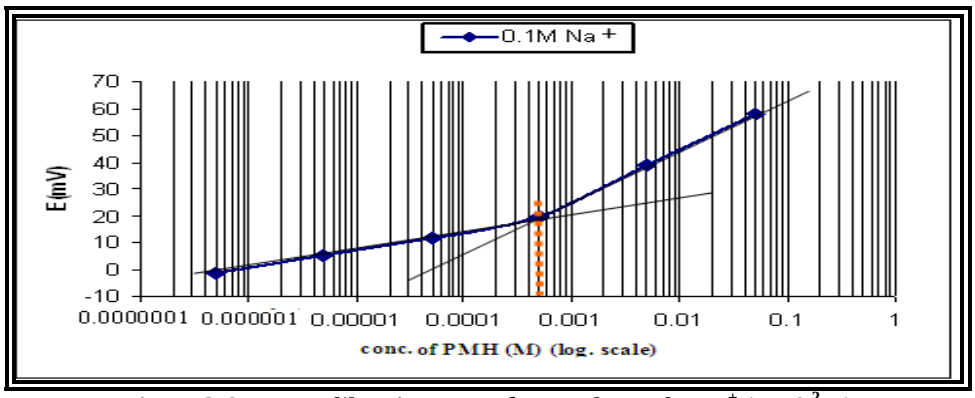


Figure 3-6: FIM calibration curve for E1 electrode, Na^+ (5×10^{-2}M) as interfering ion $a_A = 5\times10^{-4}$M.

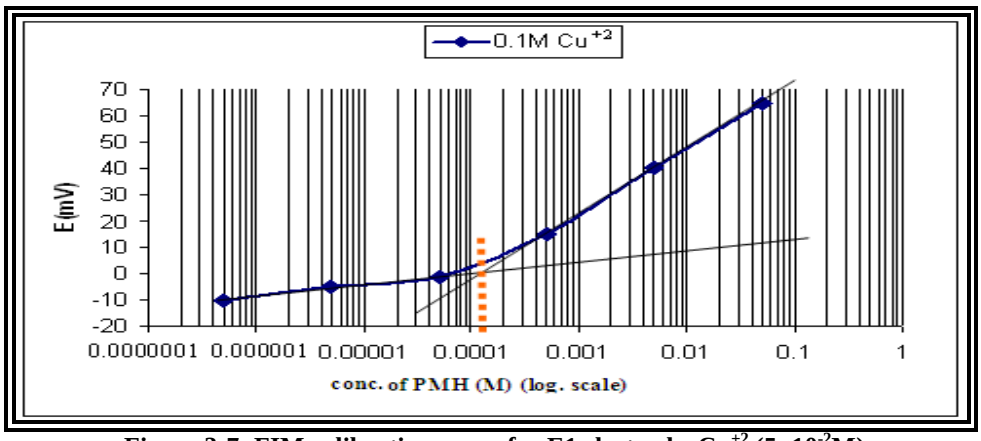


Figure 3-7: FIM calibration curve for E1 electrode, Cu^{+2} (5×10^{-2}M) as interfering ion $a_A = 1.4\times10^{-4}$M.

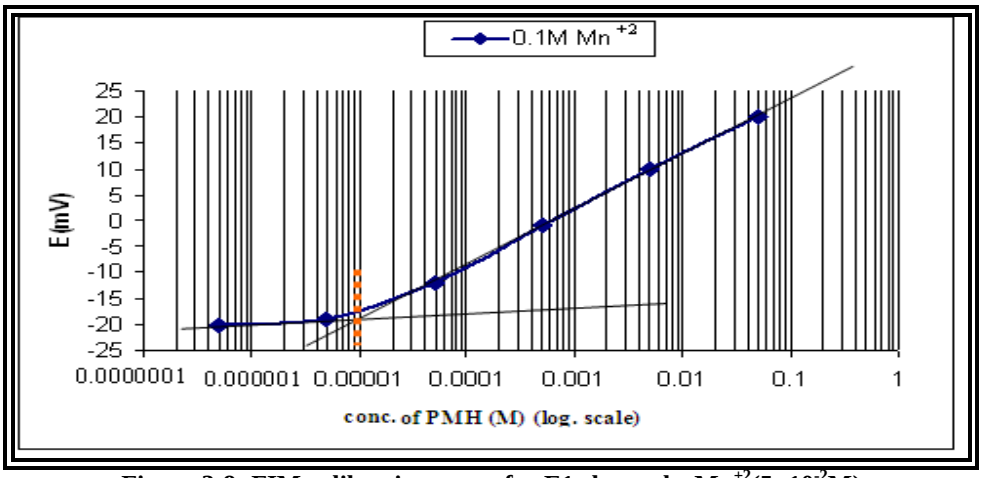


Figure 3-8: FIM calibration curve for E1 electrode, Mn^{+2}(5×10^{-2}M) as interfering ion $a_A=9\times10^{-6}$M.

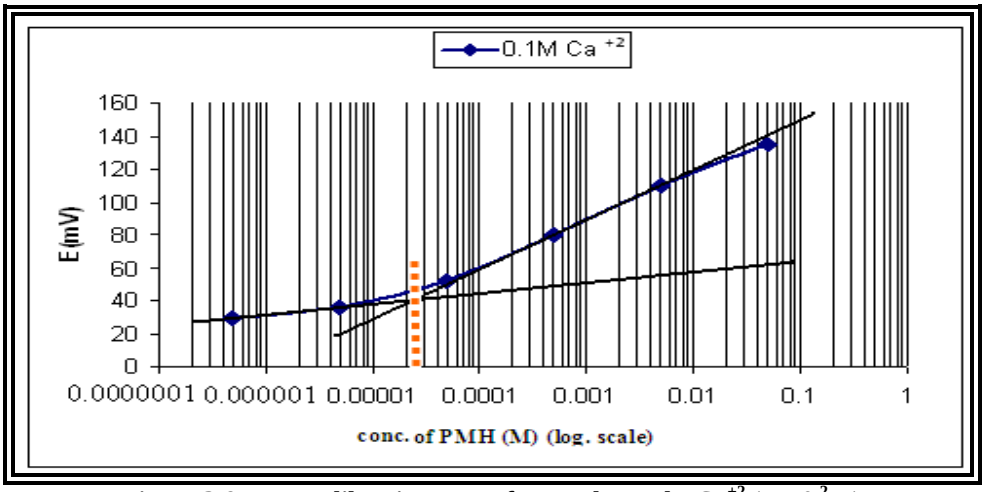


Figure 3-9: FIM calibration curve for E1 electrode, Ca^{+2} (5×10^{-2}M) as interfering ion $a_A=2.5\times10^{-5}$M.

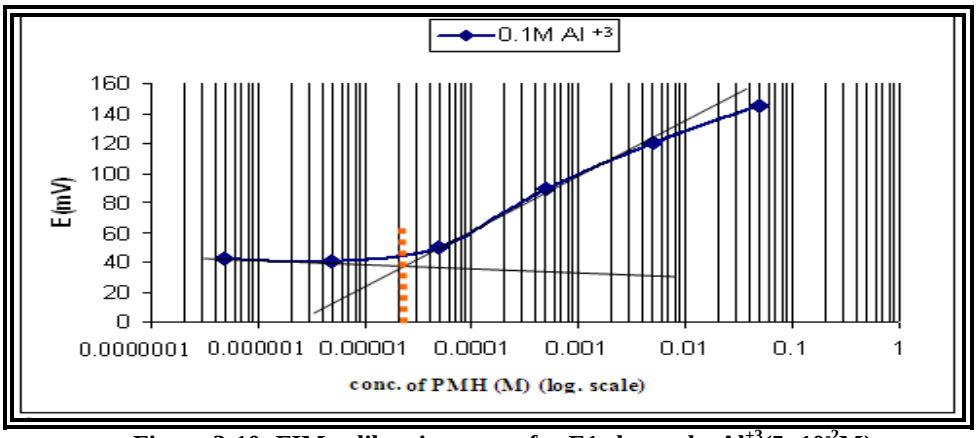


Figure 3-10: FIM calibration curve for E1 electrode, Al^{+3}(5×10^{-2}M) as interfering ion $a_A= 2\times10^{-5}$M.

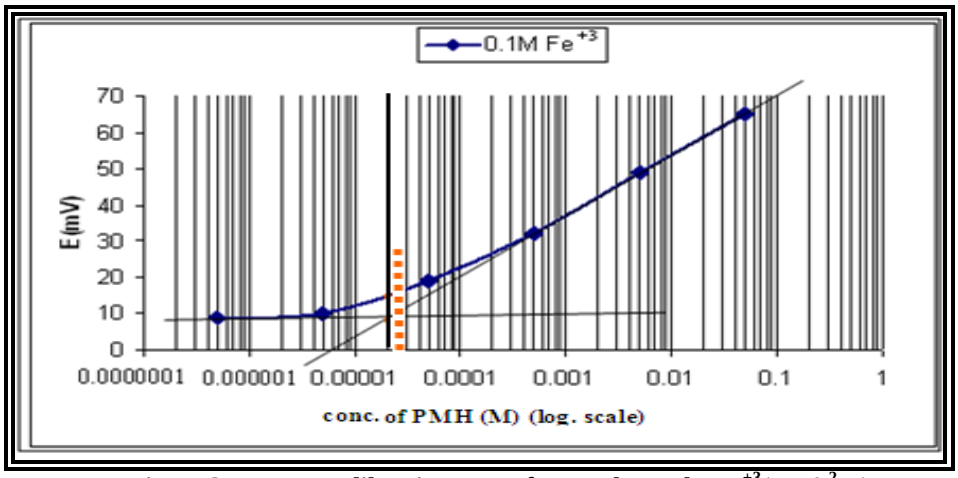


Figure 3-11: FIM calibration curve for E1 electrode, Fe^{+3}(5×10^{-2}M) as interfering ion a_A= 2.5 $\times10^{-5}$M.

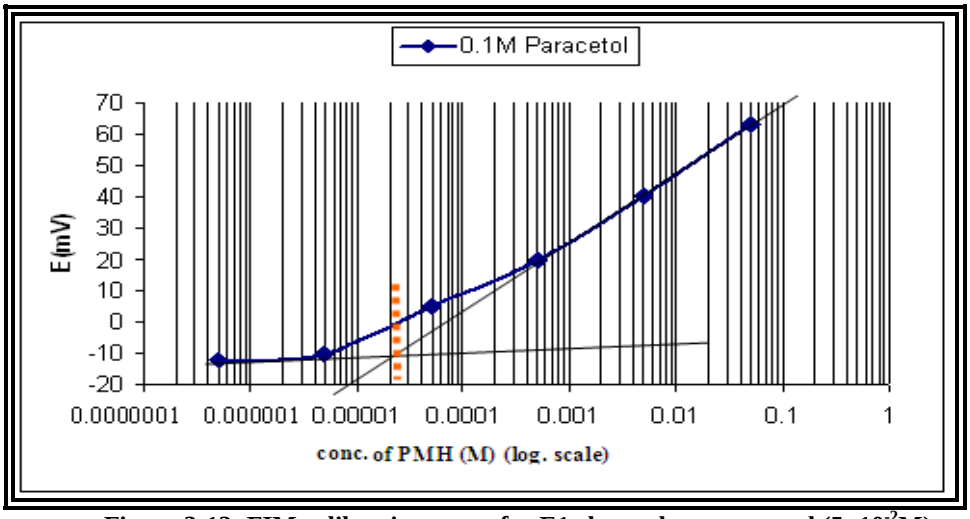


Figure 3-12: FIM calibration curve for E1 electrode, paracetmol (5×10^{-2}M) as interfering ion a_A= 2 $\times10^{-5}$M.

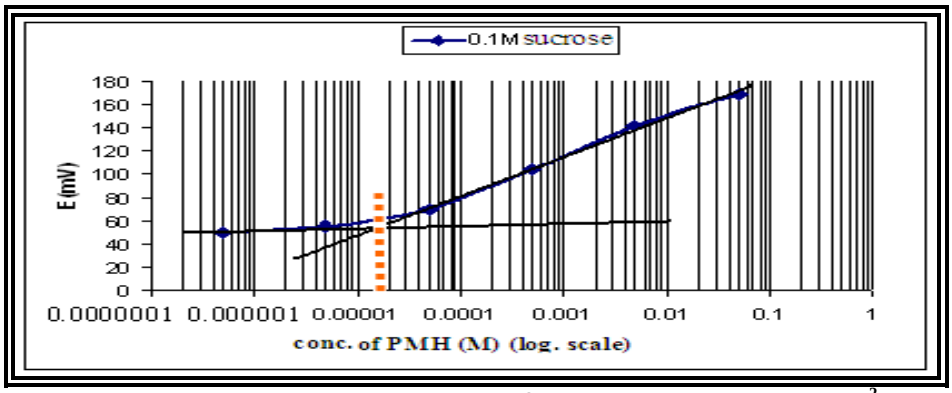


Figure 3-13: FIM calibration curve for E1 electrode, sucrose (5×10^{-2}M) as interfering ion a_A= 1.8 $\times10^{-5}$M.

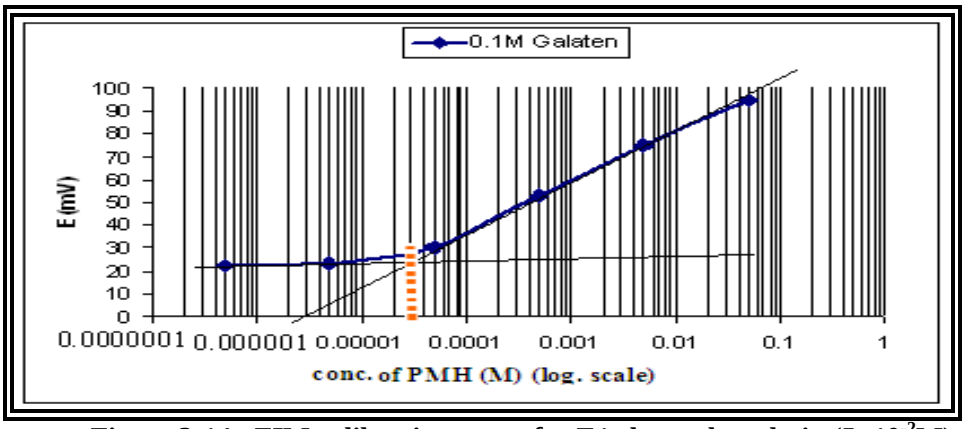


Figure 3-14: FIM calibration curve for E1 electrode, gelatin (5×10^{-2}M) as interfering ion $a_A = 3\times10^{-5}$M.

Table 3-6:- Values of $K^{pot}_{A,B}$ according to FIM, *when* $a_B = 5\times10^{-2}$ M.

Interfering Ion	$a_B = 5\times10^{-2}$ M	
	a_A	$K^{pot}_{A,B}$
K^+	3×10^{-5}	0.00060
Na^+	5×10^{-4}	0.0100
Cu^{+2}	1.4×10^{-4}	0.000632
Mn^{+2}	9×10^{-6}	0.0000402
Ca^{+2}	2.5×10^{-5}	0.000112
Al^{+3}	2×10^{-5}	0.0000537
Fe^{+3}	2.5×10^{-5}	0.0000672
paracetmol	2×10^{-5}	0.000400
sucrose	1.8×10^{-5}	0.000360
gelatein	3×10^{-5}	0.00060

3-1-5-Sample analyses:-

3-1-5-1-Direct method: -

The calibration curve was constructed (for E1 electrode) and the concentration of the unknown was calculated from the linear equation y=24.871 Ln(x) + 236.75 of the calibration curve which has the

slope (S) ± S.D. = 57.27 ± 0.0907 and the intercept ± S.D. = 236.75 ± 0.1336, for n=5, and the results are listed in Table 3-7.

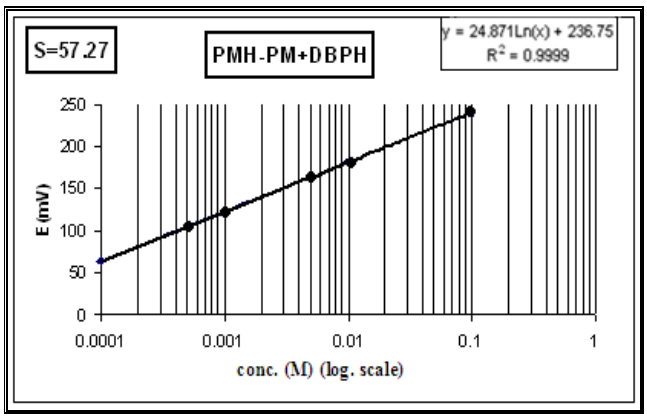


Figure 3-15:- Calibration curve of E1 electrode.

Table 3-7:- The results of five samples of promethazine hydrochloride standard solution 10^{-4} M using direct method for E1 electrode, where slope=57.27 mV/decade.

Potential reading E(mV)	conc. of (PMH) sample calculated from linear equation/(M)	S*	$\overline{X} \pm (ts/\sqrt{N})$	Re%	E_r%	RSD%
64.92	0.999×10^{-4}	3.701×10^{-7}	$0.995 \times 10^{-4} \pm 0.461 \times 10^{-6}$	99.9%	-0.1%	0.372%
64.89	0.998×10^{-4}			99.8%	-0.2%	
64.84	0.996×10^{-4}			99.6%	-0.4%	
64.77	0.993×10^{-4}			99.3%	-0.7%	
64.69	0.990×10^{-4}			99 %	-1%	

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

3-1-5-2-Incremental methods:-

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

It carried out by a procedure that 0.5 mL increment of 10^{-2}M promethazine hydrochloride as standard was added to 20 mL of sample as unknown. The results

of calculation (SAM) for the promethazine hydrochloride using (E1) electrode and equation 1-13, recovery, relative error and relative standard deviation for five additions of promethazine hydrochloride are listed in Table 3-8.

Table 3-8:- The results for five additions of promethazine hydrochloride standard solution using (SAM) for E1 electrode, where slope=57.27 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)	S*	$\overline{X} \pm (ts/\sqrt{N})$	Re%	E_r %	RSD%
0	123.0	--------	0	1	----------	5.831×10^{-6}	$0.996\times10^{-3}\pm0.727\times10^{-5}$	----------	----------	0.585%
0.5	128.0	5.0	40	1.2227	0.987×10^{-3}			98.7%	-1.3%	
1.0	131.9	8.9	20	1.4302	0.997×10^{-3}			99.7%	-0.3%	
1.5	135.2	12.2	13.3	1.6331	0.995×10^{-3}			99.5%	-0.5%	
2.0	137.9	14.9	10	1.8204	0.998×10^{-3}			99.8%	-0.2%	
2.5	140.2	17.2	8	1.9968	1.003×10^{-3}			100.3%	0.3%	

*t=2.78; N=5.

3-1-5-2-2-Multi standard addition method (MSA):-

The calibration curve for MSA for (E1) electrode was shown in Figure 3-16 by plotting antilog (E/S) versus the volume of the five additions of standard promethazine hydrochloride. 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 3-9.

Vol.(mL) of std. add	E/(mV)	Antilog (E/S)
0	123.0	140.515
0.5	128.0	171.802
1.0	131.9	200.967
1.5	135.2	229.481
2.0	137.9	255.795
2.5	140.2	280.578

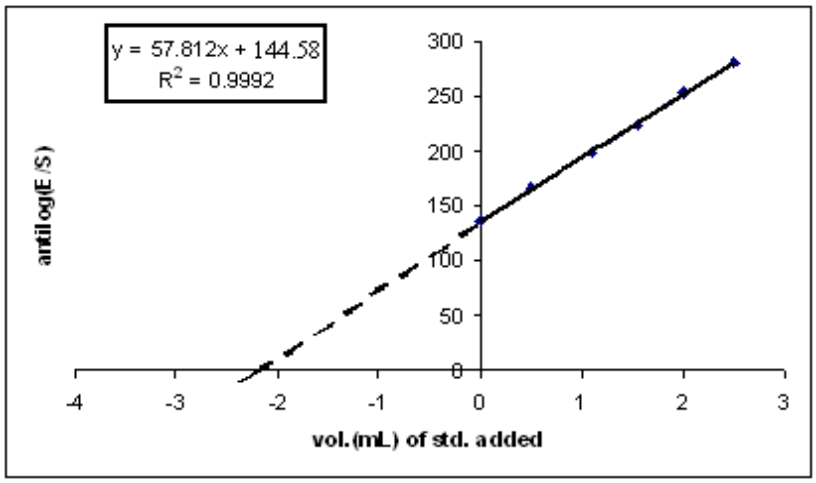


Figure 3-16:- Calibration curve of antilog (E/S) versus the volume added of standard 10^{-2}M for determination of 25 mL promethazine hydrochloride solution 10^{-3}M by (MSA).

Table 3-9:- 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= 57.812x+144.58	0.9992	2.501	1.004×10^{-3}	100.4%	+ 0.4%

3-1-5-2-3-Titration method:-

The potentiometric titration for 15 mL of 0.01 M promethazine hydrochloride sample solution with 0.01 M molybdophosphoric acid as titrant solution as shown in Figures 3-17 and 3-18, the results of titration (Re%, E_r% and RSD%) are listed in Table 3-10.

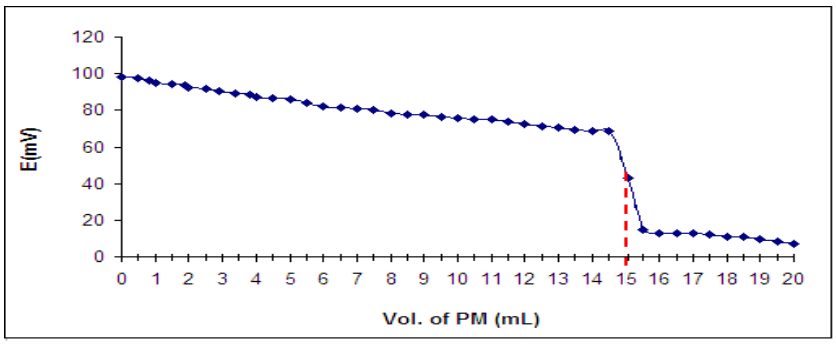


Figure 3-17:- Titration curve of E1 electrode for 15 mL sample solution 0.01 M promethazine hydrochloride with 0.01 M of PM as a titrant solution.

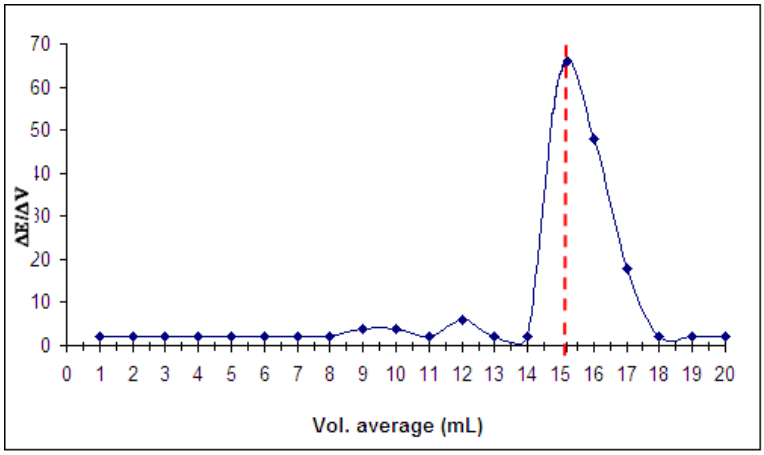


Figure 3-18:- Titration curve of E1 electrode by using first derivative, 15 mL sample solution 0.01 M promethazine hydrochloride with 0.01 M of PM as a titrant solution.

Table 3-10:-The results of using titration method for standard promethazine hydrochloride sample for E1 electrode.

Titration Figure	Vol. mL at the end point	C_U(M)	Re%	E_r%	RSD*%
Figure 3-17	14.8	0.986×10^{-2}	98.6 %	-1.33 %	0.500%
Figure 3-18	14.9	0.993×10^{-2}	99.3%	-0.7%	

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

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

Due to the vital importance of the rapid assay of pharmaceutical products, in recent years, potentiometric measurement using ion-selective electrodes has found widespread use in pharmaceuticals and clinical analyses, and in the study of drug interactions with other chemicals. The (E1) electrode was proved to be useful in the potentiometric determination of promethazine hydrochloride in pharmaceutical preparations.

3-1-6-1-Direct method:-

The calibration curve was constructed and the concentration of the unknown was calculated from the linear equation y= 24.871 Ln(x) +236.75 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^{-3}M, using direct method for E1 electrode.

E(mV) for the sample	The conc. of sample calculated(M)	S*	$\bar{X} \pm (ts/\sqrt{N})$	Re%	E_r%	RSD%
65	1.002×10^{-3}	6.364×10^{-4}	$1.003 \times 10^{-3} \pm 0.793 \times 10^{-3}$	100.2%	0.2%	0.634%
65.15	1.008×10^{-3}			100.8%	0.8%	
64.17	1.009×10^{-3}			100.9%	0.9%	
65.5	0.993×10^{-3}			99.3%	-0.7%	
65.7	1.003×10^{-3}			100.3%	0.3%	

*t=2.78; N=5.

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

It carried out by a procedure that 0.5 mL increment of 10^{-2}M promethazine hydrochloride as standard was added to 20 mL of sample as unknown. The results of calculation (SAM) by using (E1) electrode and equation 1-13, recovery, relative error and relative standard deviation for five additions of promethazine hydrochloride are listed in Table 3-12.

Table 3-12:- The results for five additions of standard solution at concentration 10^{-3}M, for E1 electrode, where slope=57.27mV/decade.

V_S(mL) added	E(mV)	ΔE	(V_U/V_S)	Antilog (ΔE/S)	C_U/(M)	S*	$\overline{X} \pm$ (ts/√N)	Re%	E_r %	RSD%
0	122	--------	0	----------	--------	9.127×10^{-6}	$0.994\times10^{-3}\pm0.114\times10^{-5}$	--------	-------	0.918%
0.5	126.9	4.9	40	1.218	1.007×10^{-3}			100.7%	0.7%	
1.0	131.0	9.0	20	1.436	0.985×10^{-3}			98.5%	-1.5%	
1.5	134.3	12.3	13.3	1.639	0.986×10^{-3}			98.6%	-1.4%	
2.0	136.9	14.9	10	1.820	0.998×10^{-3}			99.8%	-0.2%	
2.5	139.3	17.3	8	2.005	0.996×10^{-3}			99.6%	-0.5%	

*t=2.78; N=5.

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

The calibration curve for MSA for (E1) electrode was shown in Figure 3-19 by plotting antilog (E/S) versus the volume of the five additions of standard promethazine hydrochloride. 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	122	134.977
0.5	126.9	164.369
1.0	131	193.825
1.5	134.3	221.326
2.0	136.9	245.715

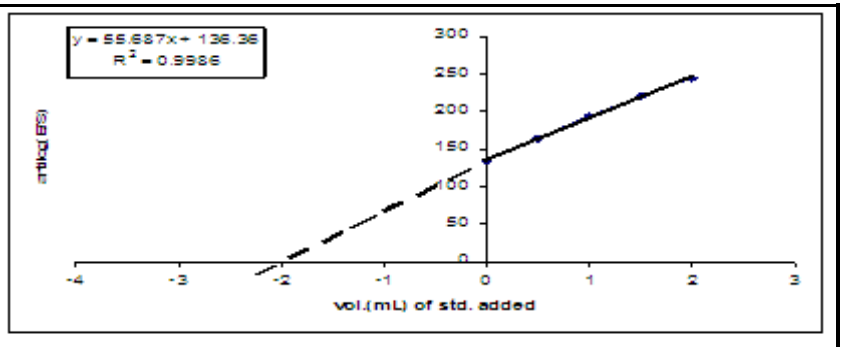


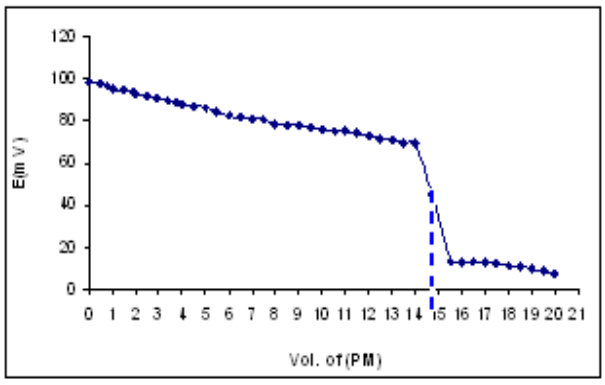
Figure 3-19:- Calibration curve of antilog (E/S) versus the volume added of standard 0.01 M for determination of 25 mL standard solution 0.001 M by (MSA) for E1 electrode.

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.

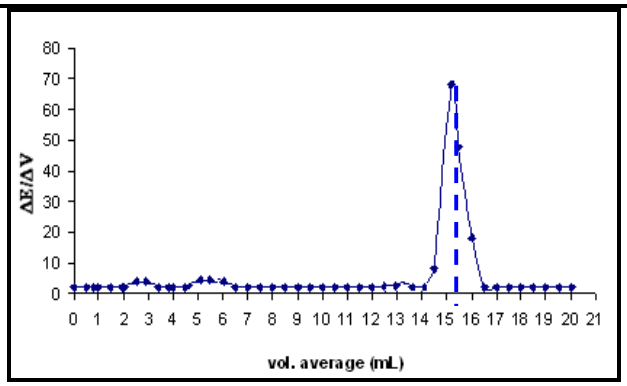
Linear equation	R	Volume at intercept (mL)	C_U(M)	Re%	E_r%
Y=55.687x+136.36	0.9986	2.45	0.980×10^{-3}	98.0%	-2.0%

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

The potentiometric titration for 15 mL of 0.001 M promethazine hydrochloride sample solution with 0.001 M of molybdophosphoric acid as titrant solution as shown in Figures 3-20-(a) and 3-20-(b), the results of titration (Re%, E_r% and RSD%) are listed in Table 3-14.



a- Titration curve



b- By using first derivative

Figure 3-20: (a)- Titration curve of E1 electrode for PMH solution containing 0.001 M PMH with 0.001 M of PM as a titrant solution, (b)- by using first derivative, for PMH solution containing 0.001 M PMH with 0.001 M of PM as a titrant solution.

Table 3-14:- The results of using titration method for E1 electrode for standard solution.

Titration Figure	Vol. mL at the end point	C_U(M)	Re%	E_r %	RSD*%
Figure 3-20-(a)	14.9	0.993×10^{-3}	99.3%	-0.7%	0.919%
Figure 3-20-(b)	15.1	1.006×10^{-3}	100.6 %	0.6 %	

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

Table 3-15:- Summary of sample analyses of coldein tablets pharmaceutical using E1 electrode.

Parameter	Direct method	SAM	MSA	Titration Method
Conc.(M)	1.000×10^{-3}	1.000×10^{-3}	1.000×10^{-3}	1.000×10^{-3}
Found(M)	1.003×10^{-3}	0.994×10^{-3}	0.980×10^{-3}	0.9995×10^{-3}
RSD*%	0.634%	0.918%	----------	0.919 %
Re%	100.3%	99.4%	98.0%	99.9 %
E_r%	0.3%	-0.6%	-2.0%	-0.1 %

RSD*% for n=5.

3-1-7-Sample analyses by using UV-spectrophotometry:-

3-1-7-1-Normal Spectroscopy:-

Normal UV spectrum of promethazine hydrochloride shows two absorption wavelengths 249 nm and 299 nm. Figure 3-21 shows the spectra for solutions ranged from 2-62 mg/L of promethazine hydrochloride. The calibration curves for promethazine hydrochloride at 249 nm and 299nm are shown in Figures 3-22 and 3-23.

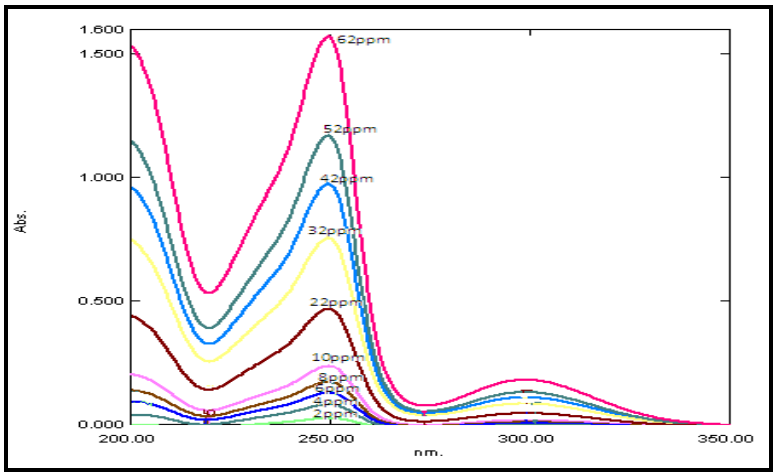


Figure 3-21:- Spectra for promethazine hydrochloride solutions at different concentration ranged from 2-62 mg/L.

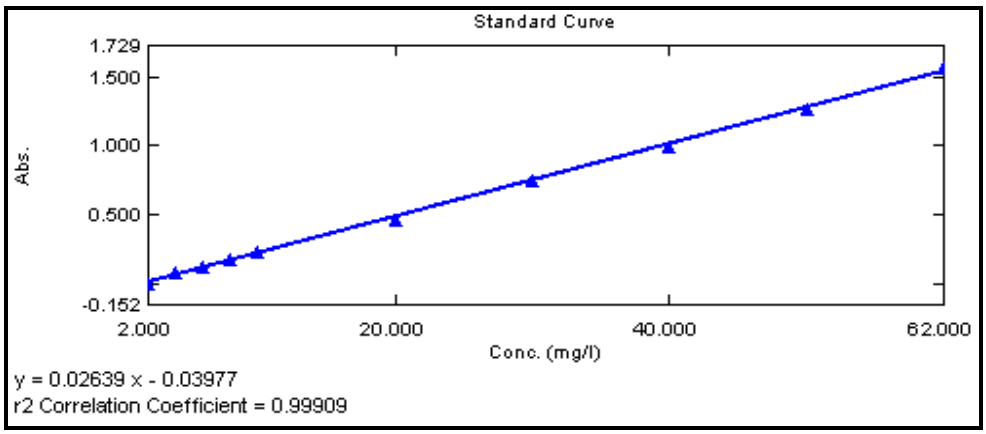


Figure 3-22:- Calibration curve for promethazine hydrochloride at λ 249nm.

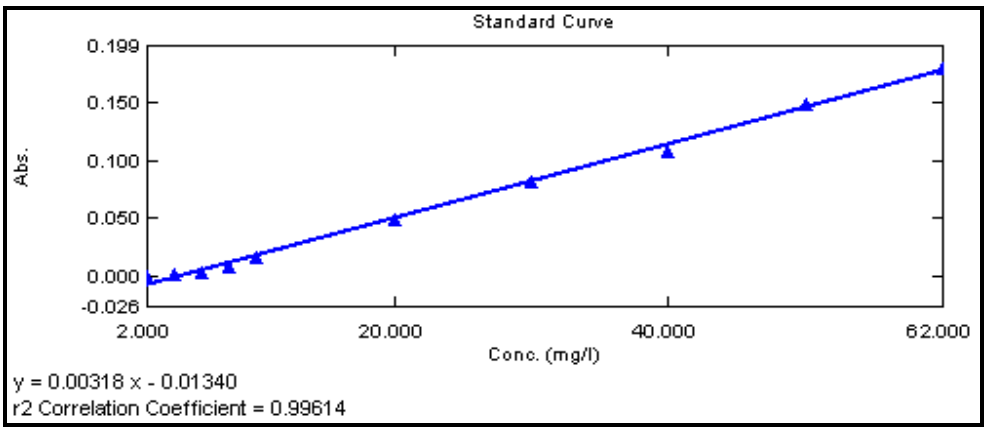


Figure 3-23:- Calibration curve for promethazine hydrochloride at λ 299nm.

Figure 3-22 used to determine prepared promethazine hydrochloride sample solutions (1×10^{-4} M that equal to 32.09 mg/L) by direct method, by reading the absorbance of the unknown samples and calculated their concentration from the linear equation of the calibration curve and confidence limit (t 95%) the results are listed in Table 3-16.

Table 3-16:- The results for five samples of promethazine hydrochloride standard solution 10^{-4}M (32.09 mg/L) by using direct method for normal calibration curve at λ_{max}.

Abs.	C_U (mg/L)	C_U (M)	S*	$\overline{X} \pm (ts/\sqrt{N})$	Re%	E_r%	RSD*%
0.787	32.090	0.999×10^{-4}	$2.881X10^{-7}$	$1.001\times10^{-4}\pm0.359\times10^{-7}$	99.9%	-0.1%	0.287%
0.788	32.035	0.998×10^{-4}			99.8%	-0.2%	
0.785	32.173	1.002×10^{-4}			100.2%	0.2%	
0.790	32.212	1.003×10^{-4}			100.3%	0.3%	
0.791	32.251	1.005×10^{-4}			100.5%	0.5%	

RSD*% for five unknown concentrations; S*: standard deviation; t=2.78; N=5.

3-1-7-2-Derivative Spectrophotometry (DS):-

3-1-7-2-1-First Derivative (^{1}D):

First-derivative (^{1}D) spectra for promethazine hydrochloride solutions 2-62 mg/L have been taken from normal using scale factor=20. Figure 3-24, shows first-derivative spectra of promethazine hydrochloride. ^{1}D spectrum of promethazine hydrochloride show a fixed peak (P) at 243nm and two fixed valley (V) at 256 nm and 211nm. But all peaks and valleys below 220 nm gave a noisy signal, which contained the absorption of impurities.

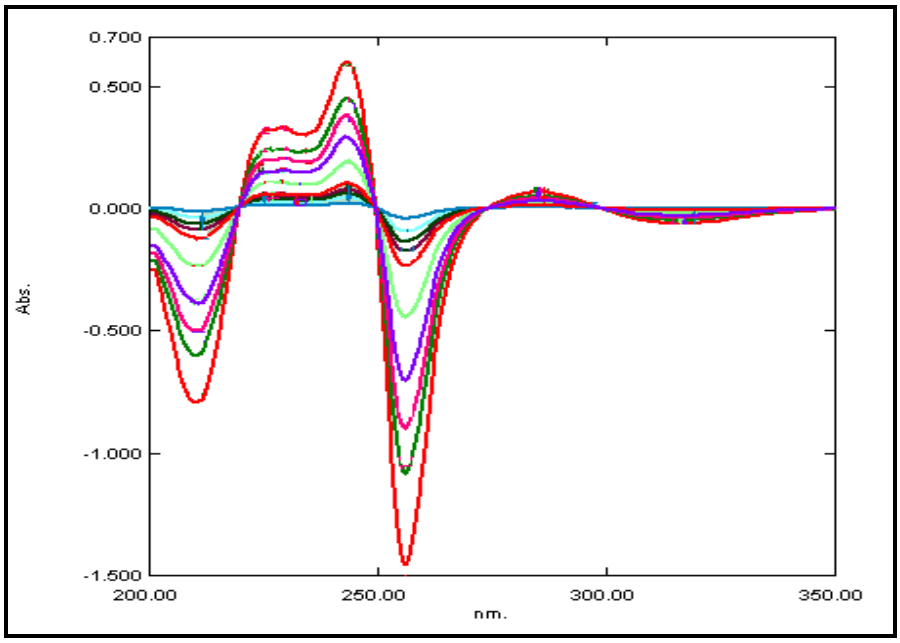


Figure 3-24:- The first derivative spectra for promethazine solutions 2-62 mg/L.

The calibration curves were constructed for these wavelengths 256 nm and 243 nm as shown in Figures 3-25 and 3-26. The calculation of the linear equations for normal and first-derivative, correlation coefficient and the range of concentrations for the calibration curves are listed in Table 3-17.

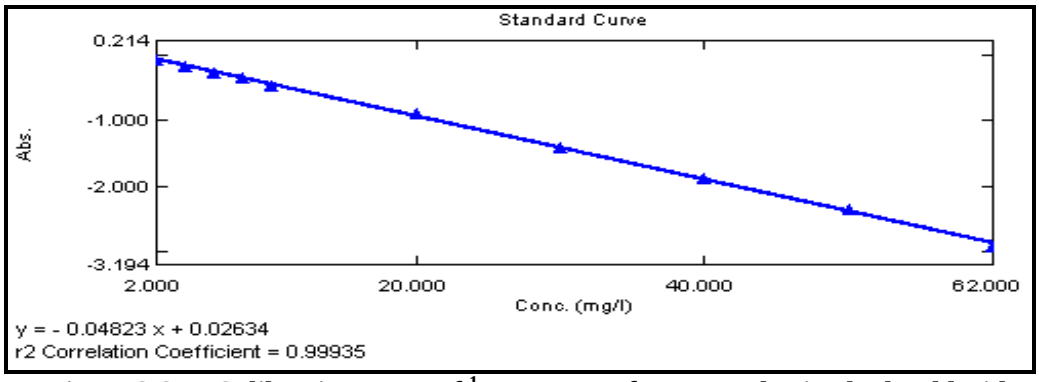


Figure 3-25:- Calibration curve of ^{1}D spectrum for promethazine hydrochloride at valley λ 256 nm.

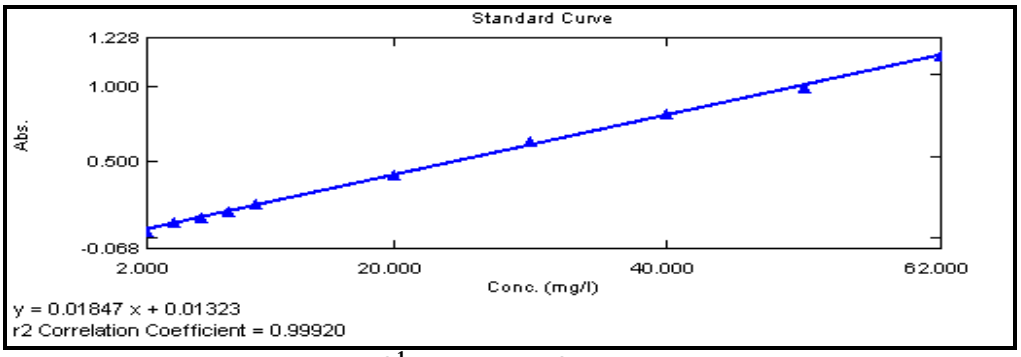


Figure 3-26:- Calibration curve of ^{1}D spectrum for promethazine hydrochloride at λ 243 nm.

Table3-17:- Calculation the t-test of the liner equation for the normal method and the first derivative.

Method	λ (nm)	Conc. Rang mg.ml^{-1}	S* for slope	S* for intercept	Y=(a±(tS/√N)) X+(b±(tS/√N))	r^2
normal	P=249	2-62	1.528×10^{-5}	2.082×10^{-5}	Y= $(0.02639\pm0.379\times10^{-5})$X+$(0.03977\pm0.517\times10^{-5})$	0.99909
	P=299	2-62	3.055×10^{-5}	4.163×10^{-5}	Y=$(0.00318\pm0.758\times10^{-5})$X+$(0.01340\pm0.103\times10^{-4})$	0.99614
^{1}D	P=243	2-62	3.407×10^{-5}	4.093×10^{-4}	Y=$(0.01847\pm0.845\times10^{-5})$X+$(0.01323\pm0.102\times10^{-3})$	0.99920
	V=256	2-62	3.214×10^{-5}	3.701×10^{-4}	Y=$(-0.04823\pm0.797\times10^{-5})$X +$(0.02634\pm0.918\times10^{-4})$	0.99935

S*: standard deviation; t=4.3; N=3.

The calibration curve of first-derivative at the λ 256 nm used to determine prepared promethazine hydrochloride sample solution (1×10^{-4}M that equal to 32.09 mg/L) by direct method, by reading the absorbance of the unknown sample and calculated the concentration from the linear equation of the calibration curve and confidence limit (t 95%) the results are listed in Table 3-18.

Table 3-18:- Calculation for five samples of promethazine hydrochloride standard solution 10^{-4}M (32.09 mg/L) by using direct method for calibration curve of ^{1}D spectra of UV-spectrophotometry.

Abs.	C_U (mg/L)	C_U (M)	S*	$\overline{X} \pm (ts/\sqrt{N})$	Re%	E_r%	RSD*%
0.747	32.090	0.999×10^{-4}	$6.324\text{x}10^{-7}$	$1.005\times10^{-4}\pm0.788\times10^{-7}$	99.9%	-0.1%	0.629%
0.748	32.145	1.001×10^{-4}			100.1%	0.1%	
0.745	32.189	1.003×10^{-4}			100.3%	0.3%	
0.750	32.324	1.007×10^{-4}			100.7%	0.7%	
0.751	32.592	1.015×10^{-4}			101.5%	1.5%	

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

3-1-8-Comparison between ISE and normal spectroscopy and first derivative (^{1}D) methods:-

The results of comparison between normal spectroscopy and first derivative (^{1}D) with direct method of ion selective electrode by using F-test are shown in the Table 3-19 and 3-20 respectively. The analytical methods results were showed to be simple, rapid and with a good precision by comparing between normal spectroscopy and first derivative (^{1}D) with direct method of ion selective electrode by using F-test at 95% confidence limit.

Table 3-19:- Calculation of F-test between the two methods ISE and UV-spectrophotometry.

C_U(M) from direct method of ISE	S*	C_U(M) from direct method of UV-spectrophotometry	S*	The (F) magnitude
0.999×10^{-4}	3.701×10^{-7}	0.999×10^{-4}	2.881×10^{-7}	1.6504
0.998×10^{-4}		1.001×10^{-4}		
0.996×10^{-4}		0.998×10^{-4}		
0.993×10^{-4}		1.003×10^{-4}		
0.990×10^{-4}		1.005×10^{-4}		

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

Table 3-20:- Calculation of F-test between the two methods ISE and first derivative.

C_U(M) from direct method of ISE	S*	C_U(M) from direct method of First Derivative	S*	The (F) magnitude
0.999×10^{-4}	3.701×10^{-7}	0.999×10-4	6.324×10^{-7}	2.9197
0.998×10^{-4}		1.001×10-4		
0.996×10^{-4}		1.003×10-4		
0.993×10^{-4}		1.007×10-4		
0.990×10^{-4}		1.015×10-4		

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

1- Standard Deviation (SD)

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

Where:

X_i = concentrations of individual deviations.

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

N = no. of degrees of freedom.

2- Relative Standard Deviation (RSD%)

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

3- Relative Error (E_r%)

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

Where:

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

4- Recovery (Re%)

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

5- **F-test**

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

Where:

S_a, S_b are the standard diviations for first and second methods respectivily, ($S_a > S_b$).

Supervisor Certification

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

Signature:
Supervisor: Dr. Khaleda Hamid M. Al-saidi
Date:

In View of the available recommendations, I forward this thesis for debate by the Examining Committee.

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Date:

Examining Committee's Certification

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

Chairman

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Name**: Dr. Abdul-Mohsin A. Al-Haideri**

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Signature:

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Acknowledgments

I wish to express my deepest gratitude and appreciation to my supervisor Dr. Khaleda H. Al-saidi for her patience, supervision and encouragement during the course of my study.

I am sincerely thankful to Dr. Salman A. Ahmed the Head of Chemistry Department at AL-Nahrain University for all the facilities that he offered during my research.

Finally, I would like to thank my parents, brothers and my sisters as well as all my friends for their support and encourage me.

Zainab Watheq Ahmed

2010

References:-

1) Toshio Nakamura," Development and Application of Ion-Selective Electrodes", *anal. Sci.*, **vol. 25**, pp. 123-137, 2009.

2) In Jun Yoon, Jae Ho Shin, Insook Rhee Paeng, Hakhyun Nam, Geun Sig Cha, Ki-Jung Paeng," Potentiometric behavior of metalloporphyrin-based ion-selective electrodes", *anal. chim. acta.,* **vol. 367**, pp. 175-181, 1998.

3) Eric, B. and Yu, Q., "Electrochemical Sensors", *anal. chem.,* **vol. 78**, pp. 3965-3984, 2006.

4) Wahl, "A Short History of Electrochemistry", *galv. tech.*, **vol. 96**, pp. 1820-1828, 2005.

5) Farnoush, F.; Mohammad, R.; Rassoul, D. and Parviz, N.,"Developments in the Field of Conducting and Non-conducting Polymer Based Potentiometric Membrane Sensors for Ions Over the Past Decade", *Sensors*, **Vol. 8**, pp. 2331-2412, 2008.

6) Skoog , D. A. , West D.M, " Principles of Instrumental analysis", *third Edition*, Saunders College publishing, Florida, **page 574**,1985.

7) Ganjali, M., Norouzi, H. Ghorbani, B. Larijani, A. Tadjarodi, Y. Hanifehpour," Glass Electeodes for Hydrogen", *anal. chem.*, **vol. 8**, pp. 233-241, 2006.

8) Eric, B.,Yu. Q., "Electrochemical Sensors", *anal. chem.*, **vol. 78**, pp. 3965- 3984, 2006.

9) Ganjali, M. R.; Ives, D., Janz, G., M.," Encyclopedia of Sensors, Potentiometric Ion Sensors", *American Scientific Publisher*, **vol. 8**, pp. 197-288, 2006.

10) Rezapour, M.; Faridbod, F.; Pourjavid P., M. R.," Supramolecular Based Membrane Sensors", *Sensors*, **vol. 6**, pp. 1018-1086, 2006.

11) Ramin M., Reza H., Hossein M., Ali H., Khalil F.," 6-Ketomethyl Phenanthridine as a New Carrier in the Construction of a Highly Selective Fe(III) Ion-Selective Membrane Electrode", *Turk. J. Chem.*, **vol. 33**, pp. 1-10, 2009.

12) Mohammad R. G., Rassoul D., Parviz N. ," Ion-Selective Electrodes", *chemical abstract* , **vol. 32**, pp.323-332, 2008.

13) Lin, Z.; Lui L. J., Chen G., Fresenius," Ion-Selective Electrode Measurements", *J. Anal. Chem.*, **vol. 37**, pp. 988-997, 2001.

14) S. Safari M., Ponnambalam R., Selvaganapathy, M. Jamal Deen, " Microfabricated True Reference Electrode for Sensing applications", *Analytica Chimica Acta* , **vol. 549**, pp. 59-66, 2005.

15) D. A. Skoog - D. M. West - F. J. Holler: Fundamentals of Analytical Chemistry, *Saunders College Publishing*, Fort Worth, **page 332**, 1992.

16) J. Kenkel, "Analytical Chemistry for Technicians, Lewis Publishers", *Boca Raton (Florida)*, pp. 265-274, 1994.

17) Solomon, S., "Sensors Handbook", *McGraw-Hill*, New York, NY, 1998.

18) Richard, P., Erno, L., "Recommendations for Nomenclature of Ion-Selective Electrodes", *Pure &App. Chem.*, **vol. 66**, pp. 2527-2536, 1994.

19) Richard P., Buck, Erno L. ," recommendations for Nomenclature of Ion Selective Electrodes", *Pure &App. Chem.*, **vol. 66**, pp. 2527-2536, 1994.

20) Rundle, C.," A Beginners Guide to Ion-Selective Electrode Measurements", Nico2000 Ltd, London, UK, 2008.

21) Farnoush F., Mohammad R., Parviz N., "The fabrication of potentiometric membrane sensors and their applications", *African Journal of Biotechnology*, **vol. 6**, pp. 2960-2987, 2007.

22) H. R. Thirsk, J. A. Harrison "A Guide to the Study of Electrode Kinetics", 1st. Ed., *Academic Press*, London and New York (1972).

23) Thomas A. D. Patko," Ion Selective Sensors and Electrodes Technologies for Industrially, Environmentally and Biologically Significant Ion Measurements", *Anal. Chem.*, **vol. 42**, PP. 714-978, 2003.

24) Baily, P., Thomas, L., "Analysis with ion selective electrodes", *Heyden and Son*, London (1976).

25) Evans, A.," Potentiometry and Ion Selective Electrodes", *John wiley & Sons*, 1987.

26) Eric B., Erno P., Philippe B.," Selectivity of Potentiometric Ion Sensors", *Anal. Chem.*, **vol. 72**, pp. 1127-1133, 2000.

27) Yoshio, U., Philippe, B., Kayoko, U., Koji, T., Shigern, A., "Selectivity Coefficients for Ion Selective Electrodes: Recmmended methods for Reporting $K_{A,B}$ values", *Pure and Appl. Chem.*, **vol. 72**, pp. 1851-2082, 2000.

28) Umezawa, Y. K. and Sato, H.,"Selectivity Coefficients for Ion Selective Electrodes", *Pure and Appl. Chem.*, **vol. 74**, No. 6, pp. 923–994, 2002.

29) S. Sadeghi, M.T. Vardini, H. Naeimi, Annali Di Chim.," Selectivity Coefficients", *Anal. Chem.*, **vol. 96**, pp. 61-65, 2006.

30) Hai Xia WANG, Min P.," A Method of Determining Selectivity Coefficients Based on the Practical Slope of Ion Selective Electrodes", *Chinese Chemical Letters*, **vol. 13**, pp. 355-358, 2002.

31) Y. Umezawa (Ed.)," Handbook of Ion-Selective Electrodes: Selectivity Coefficients", *CRC Press*, Boca Raton, FL (1990).

32) J.D.R.Thomas, P. Bühlmann, K. Umezawa, K. Tohda, S. Amemiya.," Potentiometric selectivity coefficients of ion-selective electrodes", *Pure and Appl. Chem.*, **vol. 72**, pp. 1851-2082, 2000.

33) Koji T., Diana D., Masahiro SH. , Yoshio U.," Studies on the Matched Potential Method for Determining the Selectivity Coefficients of Ion-Selective Electrodes Based on Neutral Ionophores", *Anal. Sci.*, **vol. 17**, pp. 123-131, 2001.

34) James, W., Eileen, M.," Undergraduate instrumental analysis", *New York*, ^{6}th edition, CRC Press, 2005.

35) Alun, E., "Potentiometry and ion selective electrode", *John Wiley and Sons*, (1987).

36) D.A.Skoog and D.West. , "Analytical Chemistre" 6th Ed., *Saunders Collge Publishing* , United States America, New York, **Page 332**, 1992.

37) Takashi, M., Toshihiko, I.," Potentiometric titration method for Ion-Selective Electrodes", *Analytical Communications*, **vol. 34**, pp. 257-259, 2007.

38) Maha Abdulateef yahya, "Preparation of liquid electrode based on Amiloride drug complex in PVC matrix membrane", *MSc thesis,* al-Nahrain university; 2009.

39) Thierry L. G., Jim B., Les Ebdon, David S., "Automatic continuous river monitoring of nitrate using a novel ion-selective electrode", *J. Environ. Monit.*, **vol.** 5, pp. 353-358, 2003.

40) Hak-Jin Kim, John W. Hummel, Kenneth A. Sudduth, Peter P. Motavalli, " Simultaneous Analysis of Soil Macronutrients Using Ion-Selective Electrodes", *Published in Soil Sci. Soc. Am. J.*, **vol. 71**, pp. 1867-1877, 2007.

41) Gabriela, B.; Tatiana, V.; Martin, K.; Radko, V. and Vladimír, K., *Sensors*, **vol. 8**, pp. 594-606, 2008.

42) Kong Thoo Lin, Albert, N., Mendonga M., Maria C., Branco S.," Ion Sensitive Electrodes Based on Oxaazamacrocycles as Ionophore for the Determination of Nitrate, Salicylate or Periodate Anions", *Int. Preliminary Examination Report*, **vol. 27**, pp. 331-333, 2006.

43) Christopher MM, Belknap EB, Meyer DJ, Lackey MN, Vap LM, "Comparison of methods for sodium and potassium determination in llama urine'', *Am. J. Vet. Res.*, **vol. 57**, pp. 25-30, 1996.

44) Hassan Y. Aboul-Enein, Xian X. S., Cheng J. S.," Ion Selective PVC Membrane Electrode for the Determination of Methacycline Hydrochloride in Pharmaceutical Formulation", *Sensors*, **vol. 2**, pp. 424-431, 2002.

45) Amirh S. Al-Attas," Novel PVC Membrane Selective Electrode for the Determination of Clozapine in Pharmaceutical Preparations", Int. J. *Electrochem. Sci*., **vol. 4**, pp. 9-19, 2009.

46) Sohrab E., Sahar K.," Preparation of a Fluconazole Potentiometric Sensor and its Application to Pharmaceutical Analysis and to Drug

Recovery from Biological Fluids", *Int. J. Electrochem. Sci.*, **vol. 4**, pp. 1100-1108, 2009.

47) Mohammad R. Ganjali, Taherehsadat R., Farnoush F., Siavash Riahi," Application of a New Tramadol Potentiometric Membrane Sensor as a Useful Device for Tramadol Hydrochloride Analysis in Pharmaceutical Formulation and Urine", *Current Pharm. Anal.*, **vol. 5**, pp. 28-33, 2009.

48) Nabil S. Nassory, Shahbaz A. Maki, Mutaz A. ALI," Preparation and Characterization of an Atenolol Selective Electrode Based on a PVC Matrix Membrane", *Turk. J. Chem.*, **vol. 31**, pp. 75-82, 2007.

49) Gamal Abdel-Hafiz M., Mohamed M. Hefnawy, Abdulrahman Al-Majed, " PVC Membrane Sensors for Potentiometric Determination of Acebutolol", *Sensors*, **vol. 7**, pp. 3272-3286, 2007.

50) Joaquin A. Ortuno, Vicente R., M. S. Garcia, Isabel A., Concepcion S. P.," A New Tiapride Selective Electrode and Its Clinical Application", *Sensors*, **vol. 7**, pp. 400-409, 2007.

51) Nabil S. Nassory, Abdul-Mohsin A. Al-Haideri and Israa K.M. Al-Mashhadany," Preparation and Examination of Amine and Amiloride-Ion Selective Electrodes with PVC Matrix Membranes", *Chem. Anal.*, **vol. 43**, pp. 52- 55, 2007.

52) Eman H. EL-Naby," Polymeric Membrane Sensors for the Selective Determination of Dextromethorphan in Pharmaceutical Preparations", *anal. Sci*., **vol. 24**, pp. 1409-1414, 2008.

53) K.G. Kumar, P. Augustine, S. John, " A Novel Potentiometric Sensor for the Determination of Nimesulide", *Portugaliae Electrochimica Acta*, **vol. 25**, pp. 375-381, 2007.

54) Hassan, S. and Saoudi, M., " Pharmazeutische Produkte und Kosmetica", *Anal. Sci.*, **vol. 111**, pp. 1367-1370, 1986.

55) M. Hassan, E. Elnemma. ," Methods of Control and Standardization of Drugs Containing Water-Soluble Vitamins", *Analyst*, **vol. 114**, pp. 735-737, 1989.

56) G. N. Valsami , P. E. Macheras, M. A. Koupparis," Construction of a naproxen ion-selective electrode and its application to pharmaceutical analysis", *Analyst*, **vol. 114**, pp. 387-391, 1988.

57) J. Drozd , H. Hopkala," Cyproheptadine ion-selective electrodes and their applications in some pharmaceutical formulations", *Desalination*, **vol. 163**, pp. 119-125, 2004.

58) J. Lenik, B. Marczewska, C. Wardak," Properties of ion-selective electrodes with polymer membranes for ibuprofen determination", *Desalination*, **vol. 163**, pp. 77-83, 2004.

59) Hopkala H., Drozd J., Zareba S.," Chlorprothixene ion-selective membrane electrodes development and application in pharmaceutical analysis", *Pharmazie.*, **vol. 52**, pp. 307-309, 1997.

60) G. E. Mostafa., "PVC matrix membrane sensor for potentiometric determination of cetylpyridinium chloride", *Anal. Sci*., **vol. 17**, pp. 1043-1047, 2001.

61) Gamal Abdel El-Hafeez M. ," Potentiometric PVC Membrane Sensor for the Determination of Scopolamine in Some Pharmaceutical Formulations", *Anal. Sci.*, **vol. 18**, pp. 1335-1341, 2002.

62) M. S. Rizk, Y. M. Issa, A. F. Shoukry, M. M. Abdel-Aal," New Ampicillin Selective Plastic Membrane and Coated Metal Electrodes Based on Ampicillinium Phosphotungstate Ion pair", *Anal. Letters*, **vol. 27**, pp. 1055-1062, 1994.

63) "British pharmacopoeia on CD-ROM", version 4, *Copyright by Crown Ltd.*, London, **84** (2000).

64) Mohammad R. Ganjali, Bahareh V., P. Norouzi," Promethazine Potentiometric Membrane Sensor for Promethazine Hydrochloride Pharmaceutical Analysis; Computational Study", *Int. J. Electrochem. Sci.*, **vol. 4**, pp. 740-754, 2009.

65) O. Saleh, A. El-Azzouny, H. Aboul-Enein, A. M. Badawy, "Introduction of Promethazine Hydrochloride Selective Electrodes", *Ind. Pharm.*, **vol. 19**, pp. 35-38, 2009.

66) Theia'a N. Al-Sabha, Nief R. Ahmad, Mona I. Ibrahim," Spectrophotometric Determination of Promethazine Hydrochloride via Oxidative Coupling Reaction with Sulfonic acid", *J. of Pure & Applied Sciences*, **vol. 3**, pp. 101-108, 2006.

67) H. Sanke Gowda, K. A. Padmaji," Spectrophotometric studies on platinum Promethazine hydrochloride complex", *Microchemical J.*, **vol. 25**, PP. 396-402,1980.

68) J. Karpi, ska.," Derivative spectrophotometry-recent applications and directions of developments", *Talanta*, **vol. 64**, pp. 801-822, 2004.

69) Vincek W., Hessey G. A., Constanzer M. L., Bayne W. F.," promethazine hydrochloride: Analysis by Reverse-Phase HPLC", *Pharm. Research*, **vol. 2**, pp. 143-145, 1985.

70) D. D. Borkar, V. P. Godse, Y. S. Bafana, A. V. Bhosale.," Simultaneous Estimation of Paracetamol and Promethazine Hydrochloride in Pharmaceutical Formulations by a RP-HPLC Method", *Int. J. of Chem. Tech. Research*, **vol. 1**, pp. 667-670, 2009.

71) Vanapalli, Sivarama P. K., Lakshmi P., David W.A. Bourne," Liquid Chromatographic Method for the Simultaneous Determination of Promethazine and Three of Its Metabolites in Plasma Using Electrochemical Detectors", *J. of Chromatographic Sci.*, **vol. 39**, pp. 70-72, 2001.

72) Leelavathi D., Dressler E., Soffer E., Yachetti S., Knowles A.," Determination of promethazine in human plasma by automated high-performance liquid chromatography with electrochemical detection and by gas chromatography-mass spectrometry", *J. Chromatogr.*, **vol. 12**, pp. 105-15, 1985.

73) G. Taylor, J. B. Houston," Simultaneous determination of promethazine hydrochloride by high performance liquid chromatography", *J. Chromatogr.*, **vol. 230**, pp 194-198, 1982.

74) Mohsen M. Z., Raga E. Shohiab, Mostafa ABD-EL-FATAH," Effect of Surfactants on Response of Promethazine PVC-Membranes", *Turk. J. Chem.*, **vol. 30**, pp. 307-323, 2006.

75) M. R. Ganjali, M. Hariri, S. Riahi, P. Norouzi, M. Javaheri," Promethazine Potentiometric Membrane Sensor for Promethazine Hydrochloride Pharmaceutical Analysis", *J. Electro. Sci.*, **vol. 4**, pp. 295, 2009.

76) Nabil S. Nassory, Shahbaz A. Maki, Bashaer A. AL-Phalahy, " Preparation and Potentiometric Study of Promethazine Hydrochloride Selective Electrodes and Their Use in Determining Some Drugs", *Turk. J. Chem.*, **vol. 32**, pp. 539-548, 2008.

77) Alfantazi, A. M., Moskalyk, R. R., "Processing of indium ", *Minerals Engineering*, **vol. 16**, pp. 687-694, 2003.

78) C. Li, D.Z., X. Liu, S. Han, T. Tang, J. Han, C. Zhou," Indium Oxide nanowires as chemical sensors", *Appl. Phys. Lett.*, **vol. 82**, pp. 1609-1613, 2003.

79) K . J. Bachmann," Properties, Preparation and Device Application of Indium sulfide ", *Ann. Rev. Mater. Sci*., **vol. 11**, pp. 441-84, 1981.

80) Ashraful G. B., Akihiro H., Akio Y. ," Indium nitride (InN): A review on growth, characterization, and properties", *J. Appl. Phys.*, **vol.** 94, pp. 2769-2779, 2003.

81) Kenneth N. H., Siddartha K., Kiwoon P., Ho-min K. ," Recovery of Indium from Indium/Tin Oxides Scrap by Chemical Precipitation", *Geosystem Eng.*, **vol. 5**, pp. 93-98, 2002.

82) J. C. Manifacier," Method for forming indium oxide/n-silicon heterojunction solar cells ", *Appl. Phys. Lett.*, **vol. 31**, pp. 459-462, 1977.

83) Akiyo T., Miyuki H., Minoru O., Naohide I., Takahiro U. K.," pulmonary toxicity of indium-tin oxide and indium phosphide after intratracheal instillations into the lung of hamsters", *J. of Occupational health*, **vol. 44**. pp. 299-102, 2002.

84) I. S. Burns, J. Hult, C. F. Kaminski," Diode laser induced fluorescence spectroscopy for combustion Thermometry", *Phy. J.*, **vol. 15**, pp. 201-206, 2005.

85) F. Capitán, A. Navalón, J. L. Vilchez, L. F. Capitán-Vallvey, "Spectrofluorimetric determination of traces of indium with 5-chiorosalicylidene-*o*-aminophenol ", *J. Microchimica Acta*., **vol. 103**, pp. 5-6, 1991.

86) Justyna P.," A Sensitive Spectrophotometric Method for Determination of Trace Quantities of Indium in Soil", *J. Phy.*, **vol. 13**, pp. 7-13, 2007.

87) Narinder K. Agnihotri, Sonia Ratnanii, Vinay K. Singh, Har B. Singh," Simultaneous Determination of Gallium and Indium with 2-(5-Bromo-2-pyridylazo)-5-diethylaminophenol in Cationic Micellar Medium Using Derivative Spectrophotometry", *Anal. Sci.*, **vol. 19**, pp. 12-97, 2003.

88) N. Memon, M. I. Bhanger," Micellar Liquid Chromatographic Determination of Aluminum as its complex with 8-Hydroxyquinoline-5-Sulfonic acid ", *Acta Chromatographic*, **vol. 14**, pp. 123-127, 2004.

89) Saad S. Hassan, Wagiha H. M., Mohamed A. F. Elmosallamy, Mahra H. Almarzooqi," Novel Ibuprofen Potentiometric Membrane Sensors Based on tetraphenylporphrinato indium(III) ", *Ana. Sci.*, **vol. 19**, pp. 675-679,2003.

90) Najwa I. Abdulla, Abdul-Muhsin Al-Haideri, Moen I. Al-Joboury, Nabil S. Nassory," Construction and Characterization of Indium Liquid Ion Selective Electrodes Based on Crown Ethers in a PVC Matrix Membrane", *Turk. J. Chem.*, **vol. 29**, pp. 687- 696, 2005.

91) Brittain, E., George, W., Wella, C.," Introduction to Molecular Spectroscopy", Academic Press, London, 1987.

92)Trabelsi, H., Raouafi, F., Liman, M., Bouzouita, K.," Spectrophotometry methods and their Application" , *J. Anal. Chem.*, **vol. 21**, pp. 327-341, 2005.

93) R. N. Feudale, N. A. Woody, H. Tan, A. J. Myles, S. D. Brown, J. Ferre," Application of Derivative Spectrophotometry", *Chemom. Intell. Lab. Syst.*, **vol. 64**, pp. 178-181, 2002.

94) T. C. O'Haver, T. Begley," Signal-to-noise ratio in higher order derivative spectrometry", *Anal. Chem.*, **vol. 53**, pp. 1876–1878, 1981.

95) R. N. Ojeda, F. S. Rajas, J. M. C. Pavon," Developments of Derivative Spectrophotometry Methods", *Talanta,* **vol. 42**, pp. 1181-1195.1995.

96) Abdel-Aziz Y. EL-Sayed, Najeb A. EL-Salem," Recent Developments Derivative Spectrophotometry and Their Analytical Application", *anal. sci.*, **vol. 21**, pp. 595-614, 2005.

97) Craggs, A.; Moody, G. and Thomas J., Chem. Educ., Vol. 51, No. 8, pp. 541- 547, 1974.

98) Ibthaj Kadhim Malih," A Study on new Metoclopramide Hydrochloride membrane electrodes", *MSc thesis*, Ibn Al-Haitham; 2009.

99) R. K. Mahajan, R. Kaur, I. Kaur, V. Sharma and M. Kumar," Novel Copper (II)-Selective Electrode Based on 2,2': 5',2''-Terthiophene in PVC Matrix", *Anal. Sci.*, **vol. 20**, pp. 811, 2004.

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Construction and Study of New Ion Selective Electrodes for the Determination Promethazine Hydrochloride and Indium (III)

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

By
Zainab Watheq Ahmed

B.Sc. in Chemistry (Al-Nahrain University 2005)

Supervised by
Assistant professor
Dr. Khaleda H. Al-Saidi

2010 *1431*

الإهداء

الى الشمعة التي أحترقت لتنير دربي.....
الى من غرس في نفسي الامل.....
الى القلب الكبير....

والدي العزيز

الى من بنت فاعلى الله مقامها....
الى من زرعت فحصدت طيب ثمارها....
الى من سهرت وافنت سني عمرها....

أمي الغالية

الى من تقر بهم عيني....
الى من برؤيتهم يزول همي....
الى من بحبهم أستمد عزمي....

أخوتي وأخواتي

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

زينب

بِسْمِ اللهِ الرَّحْمَنِ الرَّحِيمِ

رَبَّنَاءَاتِنا مِنْ لَّدُنكَ رَحْمَة ً وَهَيِّئْ

لَنَا مِنْ أَمْرِنَا رَشَداً

صَدقَ اللهُ العَظيم

سورة الكهف / جزء من آية 10

جمهورية العراق
وزارة التعليم العالي والبحث العلمي
جامعة النهرين/كلية العلوم
قسم الكيمياء

تصنيع ودراسة اقطاب انتقائية جديدة لتقدير كل من البروميثازين هيدروكلورايد والاندبوم الثلاثي

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

من قبل
زينب واثق أحمد
بكالوريوس كيمياء 2005 (جامعة النهرين)

تحت إشراف
أ.م.د. **خالدة حميد محمد السعيدي**

1431 هـ ٢٠١٠ م