Republic of Iraq
Ministry of Higher Education and Scientific Research
Al-NahrainUniversity
College of Science
Department of Chemistry

Construction of new MIP-Ion Selective Electrodes for Warfarin Sodium

A Thesis

Submitted to the College of Science, Al-NahrainUniversity as a Partial Fulfillment of the Requirements for the Degree of Master of Science in Chemistry

By

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June 2016 **Ramadan 1437**

بِسْمِ اللهِ الرَّحْمَنِ الرَّحِيمِ

"يرفعُ اللهُ الذينَ آمنوا مِنكم والذينَ أوتوا العلمَ درجات"

صَدَقَ ٱللَّهِ العليُ العَظيمْ

سورة المجادلة الآية (١١)

الاهداء

إلى الذي لم يأل جهدا في تربيتي منذ الصغر...
الى الذي علمني العطاء بدون انتظار...
إلى من أحمل أسمه بكل افتخار...

ابي الغالي

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

امي الغالية

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

زوجي العزيز

الى من اشد بهم ازري في الحياة...
الى من هم بلسم جراحي...

اخواتي
فرح ودعاء

إلى كل من فرح بي وشجعني على هذه الدراسة ..

الاصدقاء والأقارب

إليهم جميعا اهدي ثمرة جهدي عرفانا بفضلهم...

ميسم

Acknowledgments

First of all, thanks to **Allah**, the Almighty, who has granted me the strength and patience to finish this work.

I wish to express my deepest gratitude and appreciation to my supervisor **Asst. prof Dr. Yehya K. Al- bayati** for his fruitful supervision, guidance, valuable suggestions, great help and encouragement during the research course. I am sincerely thankful to **Asst. professor Dr. Nasreen R . Jber** the Head of Chemistry Department at AL-Nahrain University for all the facilities that she offered during my research, and I would like to thank **Dr. Khaleda H. Al-saidi**, great and special thanks are due to senior researcher **Dr.Nabil S. Nassory** for his valuable help and assistance during my work. I would like to thank every one who helped me to finish this thesis. All my dearest friends especially**,Sumayah,Marwah,Noor**.Finally, my special thanks and sense of gratitude are due to my family.

Maysam Ayad Hussain

2016

SUMMARY

This piece of research includes three main chapters .

Chapter one includes an introduction on ion selective electrodes (ISEs) and their work, properties, classification of ion selective membranes, cell design of ion-selective electrode and characterization of ion-selective electrodes such as selectivity coefficient with different method (separation solution method) and (matched potential method) with range of linear response, detection limit, response of time. Molecularly imprinted polymers (MIP) Technique and Approaches for preparing Molecularly Imprinted Polymers (Covalent Imprinting Method, Non-Covalent Imprinting Method). MIP component and Factors influencing polymerization (Template molecule, Functional monomer, Cross linker, Initiator and Solvent). Factors that control the synthesis of selective MIP preparation methods of MIPs Bulk polymerization and polymerization precipitation, and analytical Methods for drug estimation using the (ISEs) and (MIPs), direct method, standard addition method, multiple standard addition method and titration method. The research work covers in detail a comprehensive of a full survey of the chemical literatures related with project title. Warfarin sodium is an anticoagulant drug, which competitively depresses the synthesis of vitamin K-dependent coagulation factors. Presence of coumarin ring makes Warfarin a good complexing ligand. Coumarin complexes are of significant interest because of their biological and complexing ability .

Chapter two comprises a complete description for the chemicals used, their preparations, in addition to instruments and equipments, cell design of ion selective electrode , molecularly imprinted polymers and casting the membrane.

Summary

Chapter three consists of two methods.

1- Ion selective electrodes ISEs :

warfarin sodium ion selective electrodes have been prepared based on dodeca-molybdo phosphoric acid (MPA) and dodeca–Phosphotungstic acid (PTA) as ion-exchanger using many plasticizers which were: oleic acid (OA), tri-n-butylphosphate(TBP), Nitrobenzen (NB), Acetophenone (AP) and di-octyl phthalate (DOPH) in PVC matrix membranes. The matrix membrane was formed by mixing an appropriate plasticizer and drug complexes with PVC. The following electrode parameters including; concentration range, slope, detection limit, life time, correlation coefficient and the working pH range, also interferences were studied via selectivity against monovalent, divalent and trivalent such as (K^+, Na^+,Ca^{2+} ,Mg^{2+},$Al^{3+}$and Fe^{3+})and also use amino acid such as (alanine, proline and serin) for all the electrodes are studied by using separation (SSM) and match (MPM) methods to determine the selectivity potential coefficient ($K^{pot}_{A,B}$). The results showed that membranes of the electrodes; WFN-MPA+OA, WFN-MPA+TBP, WFN-MPA+NB , WFN-MPA+AP and WFN-MPA+DOPH gave linear dynamic response range between 1×10^{-1} and 1×10^{-5} M with nernstian slopes of 21.28–31.57 mV/decade concentration and a detection limit of (7×10^{-6} - 2×10^{-5}) M are obtained, the lifetime was (7-35) days ,correlation coefficient of 0.9969 and 0.9998, respectively. The working pH ranges were ranged from (2.5 – 10.0).And The results showed that membranes of the electrodes; WFN-PTA+OA, WFN-PTA+TBP, WFN-PTA+NB , WFN-PTA+AP and WFN-PTA+DOPH gave linear dynamic response range between 1×10^{-1} and 1×10^{-5} M with nernstian slopes of 20.04 _29.62 mV/decade and a detection limit of (6×10^{-6} _ 4×10^{-5}) M are obtained , the lifetime was (10 - 40) days ,correlation coefficient of (0.9984 and 0.99949), respectively. The working pH ranges were ranged from (3.5 – 10.0).The practical utility of electrodes have been used as indicator electrodes in the potentiometric determinations of warfarin sodium , using direct and incremental methods with successful and good results. Also these electrodes were used to determined warfarin sodium in the pharmaceutical samples.

Summary

2-Molecularly Imprinted Polymers (MIPs) : In this method warfarin sodium molecularly imprinted polymer have been prepared based on acrylamide and metha acrylic acid as monomers, ethylene glycol dimethacrylate as cross-linker and benzoyl peroxide as initiator, using two plasticizers which were: Tritolyl phosphate (TP), Di butyl sebacate (DBS) in PVC matrix membranes. The matrix membrane was formed by mixing an appropriate plasticizer and polymers with PVC. The following electrode parameters including; concentration range, slope, detection limit, life time, correlation coefficient and the working pH range, also interferences were studied via selectivity against monovalent, divalent and trivalent such as (K^+ ,Ca^{2+} and Al^{3+}) and also use amino acid (alanine,proline,serine) for all the electrodes are studied by using separation solution method (SSM) and match potential method (MPM) methods to determine the selectivity potential coefficient ($K^{pot}_{A,B}$). The results showed that membranes of the electrodes; WFN-MIP(ACY)+TP, WFN-MIP(ACY)+DBS, WFN-MIP(MAA)+TP,WFN-MIP(MAA)+DBS gave a Linear dynamic response range between 1×10^{-1} and 1×10^{-5} M, with slopes of (51.80-58.41) mV/decade ,The limit of detection of (4×10^{-6} - 3×10^{-5}) M, the lifetime were about (30,45 days) correlation coefficient (0.9987 - 0.9996). respectively. The working pH ranges were ranged from (3.5 – 9.5).

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ISE	Ion-selective electrode
WFN	Warfarin sodium
MPA	Dodeca- molybdo Phosphoric acid
PTA	Dodeca–Phosphotungstic
WFN-MPA	Warfarin sodium-molybdo phosphoric complex.
WFN-PTA	Warfarin sodium- Phosphotungstic complex.
OA	Oleic acid
TBP	Tri-butylphosphate
NB	Nitro benzene
AP	Acetophenone
DOPH	Di-octylphthalate
TP	Tritolyl phosphate
DBS	Di butyl sebacate
ACY	Acrylamide
MAA	Meth acrylic acid
EGDMA	Ethylene glycol dimethacrylate
BPO	Benzoyl peroxide
PVC	Polyvinyl chloride
THF	Tetra hydrofuran
MIP	Moleculary Imprinted Polymers
NIP	Non Imprinted Polymers
cST	stock unit of viscosity gm/sec.cm.density
e.m.f	Electromotive force

RSD	Relative standard deviation
RE	Relative error
Rec.	Recovery
FTIR	Fourier transform infrared spectroscopy
SEM	Scaning Electron Microscopy
HPLC	High performance liquid chromatography
LC	liquid chromatography
SCE	Saturated calomel electrode
SHE	Standard hydrogen electrode
FIM	Fixed interference method
FPM	Fixed primary ion method
MPM	Match potential method
TSM	Two solution method
SAM	Standard addition method
MSA	Multi Standard addition method
Std.	Standard

1.1. Ion Selective electrode

An ion-selective electrode (ISE) also known as specific ion electrode, , is a sensor that converts the activity of a specific ion dissolved in a solution in to an electrical potential which can be measured by a voltmeter or pH meter .Ion selective electrodes are generally based on highly selective ionophores embedded in hydrophobic membranes. They are usually contacted with aqueous electrolytes conductive wire and an internal or external reference. Analyte recognition process takes place followed by the conversion of chemical information into an electrical or optical signal. The ionophore is primarily responsible for the ion selectivity of the sensor by selectively and reversibly binding the analyte of interest. With optimized membrane formulations, the measured zero-current membrane potential can be directly related to the free ion activity of the analyte in the sample .[(1)]

ISE measure the concentration of ions in equilibrium at the membrane surface. In dilute solutions, this is directly related to the total number of ions in the solution but at higher concentrations, inter ionic interactions between all ions in the solution (both positive and negative) tend to reduce the mobility and thus there are relatively fewer of the measured ions in the vicinity of the membrane than in the bulk solution. Thus, the measured voltage is less than it would be if it reflected the total number of measured ions in the solution. This causes erroneously low estimates of the ion concentration in samples with a high concentration or a complex matrix. The activity coefficient is always less than one and becomes smaller as the ionic strength increases; thus the difference between the measured activity and the actual concentration differs at higher concentrations. This effect causes problems with ion selective electrode measurement. It has been observed that when plotting a calibration graph using concentration units, the line is seen to deviate from linearity as the concentration increases (it remains straight, up to the highest concentrations if activity units are used).[(2)]

1.2 Basic Theory of ISE Measurements

Ion-selective electrodes (ISE) are electrochemical transducers that respond selectively ,directly, and continuously to the activity of the free ion of interest in solution. Theoretical and practical aspects of ISE technology and methodology are reviewed regularly by Koryta every 2-3 years.[3] The electromotive force ($\mathbf{E}_{cell}$) of an electrochemical cell consisting of an ISE for the ion i and a reference electrode is described by the Nernest equation :

$$\mathbf{E_{Cell} = E_{constsnt} - 2.303\ RT/nF\ log\ a_i} \qquad \text{....1-1}$$

Where $\mathbf{E_{Cell}}$ = the total potential (mV) developed between the sensing and reference electrodes.

$\mathbf{E_{constsnt}}$ = a constant for a given cell.

R = The ideal gas constant (8.314 joule $mole^{-1}$ K^{-1}).

T = Temperature in Kelvin 298K (25^0C).

n = Ionic charge.

F = Faraday constant (96500 coulombs)

$\mathbf{a_i}$ = Activity of the ion .

Besides the membrane electrodes selective to the common inorganic anion and cation , which are commercially available , a great number of $\mathbf{ISE_S}$ have been constructed by several research groups which are selective to organic ions of pharmaceutical interest.[4] Ion-selective electrodes have some inherent advantages , such as ,sufficient selectivity and sensitivity ,wide analytical range of analyte concentrations ,insensitivity to optical interferences ,low cost ,fast response ,and flexibility in constructing flow-through sensors for analyzers.[5,6]

1.3 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. (7)

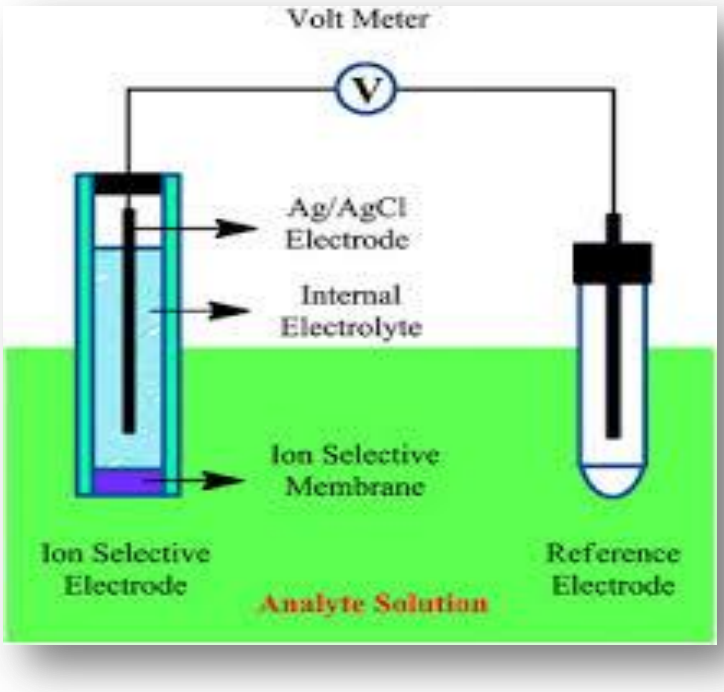


Figure (1.1): A classical ion selective electrode in electrochemical cell (7)

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 [7]:-

External ref. | testsolution | membrane | internalsolution | internal ref.

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 [8].

$$E_{total} = E^0 + E_{junction} - E_{membren} \quad \ldots 1\text{-}2$$

1.4 Classification of ion-selective electrodes

Classification of membrane selective electrode depend on physical and chemical nature of the active material from which the membrane is made :[9]

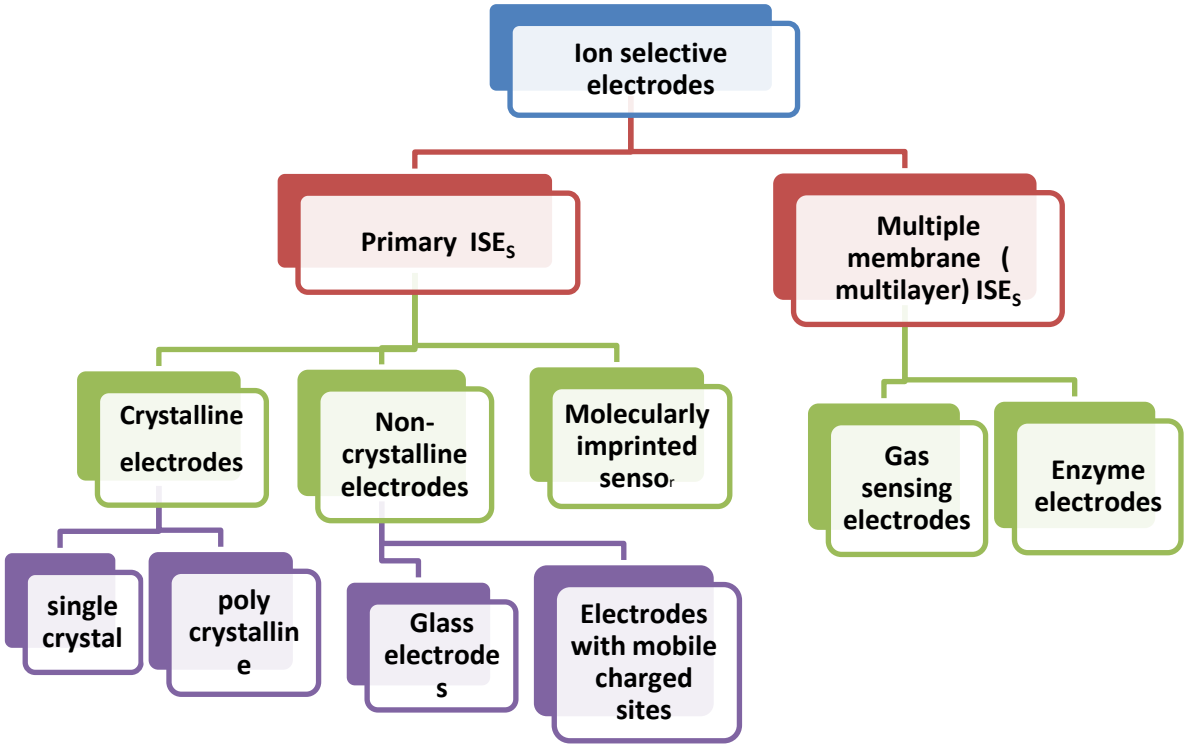


Figure (1.2): Classification of ion-selective electrodes .

1.5.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.(10)

1.6. Characterization of ion-selective electrode:

The properties of an ion-selective electrode are characterized by parameters like:

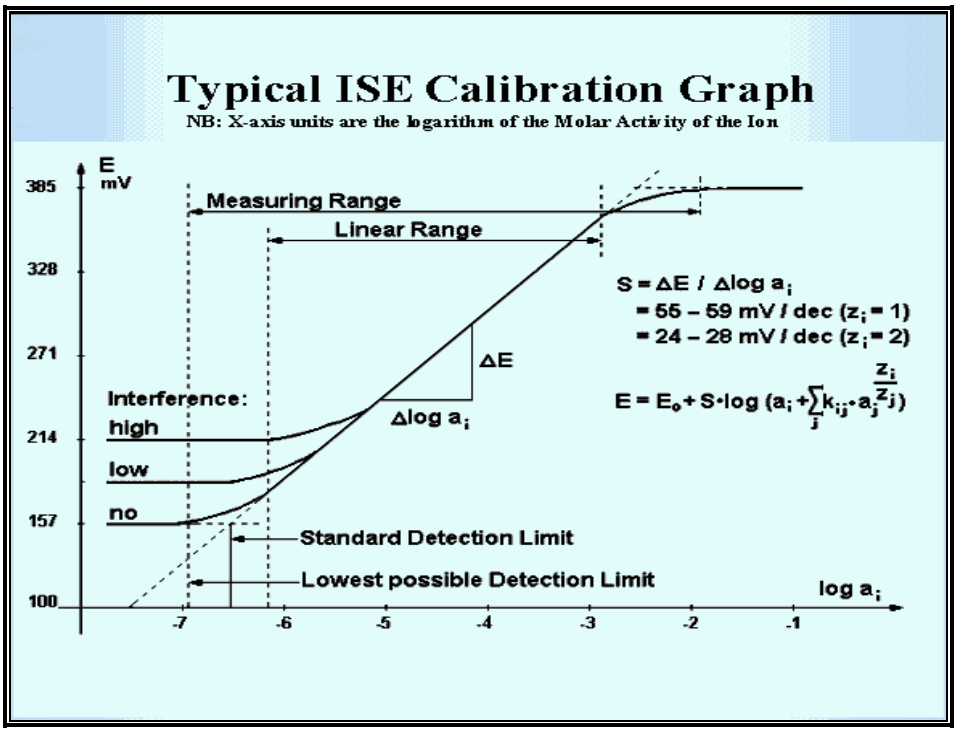
1.6.1 Calibration curve:-

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 immersed in the same solution, and the logarithm of the activity of the ions in the solution(11). This relationship is described by the Nernst equation as …. 1-1:

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

Figure 1-3 shows, a typical plot of the electrochemical cell (i.e. the potential difference measured between the ISE and the external RE of a given ion-selective electrode cell assembly) versus the logarithm of the single ionic activity (concentration) of a given species.(12)

It is recommended that the electrochemical cell is ascribed to the ordinate (vertical axis) with the more positive potentials at the top of the graph and that pa_A (-log activity of the measured species A) or pc_A (-log concentration of the measured species A) is ascribed to the (horizontal axis) with increasing activity or concentration to the right[1].The linear rang is a part of the calibration curve through which a linear regression would demonstrate that the datapoints do not deviate from linearity by more than 2 mV(13).



Figure(1.3): Typical ISE calibration graph[12].

1.6.2 Slope:

Slope is the linear part of the measurement calibration curve of the electrode. The theoretical value according to the Nernst equation is 59.16 mV/decade at 298 k for a single charge ion or 59.16/2 = 29.58 mV/decade for double charged ion. However, in certain applications, that value of the electrode slope is not critical and its value does not exclude its usefulness.[14]

1.6.3 Detection limit :

According to the IUPAC recommendation, the detection limit is defined by cross section of the two extrapolated linear parts of the ion selective calibration curve. In practice detection limit of the order of 10^{-4}-10^{-6} M is reported for most of ion selective electrodes. The observed detection limit is often governed by the presence of other interfering ions or impurities. If, for example, metal buffers are used to eliminate the effects which lead to the contamination of very dilute solutions, it is possible to enhance the detection limit down to 10^{-5} M.[15]

1.6.4 Range of linear response :

The linear range of the electrode is defined as that 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 M down to 10^{-6} or even 10^{-7} M [(16)]

1.6.5 Response time:

In earlier IUPAC recommendations, it was defined as the time between the instant at which the ion selective electrode and a reference electrode are dipped in the sample solution and the first instant at which the potential of the cell becomes equal to its steady-state value within ±1mV for the final equilibrium potential. Generally electrodes with liquid ion-exchanger membrane have longer response time than solid membraneelectrode. This may be due to the slow rate of reaction between the determined ion and the ion-exchanger which lead to slower transport of the ions across the membrane-solution interface. However, the main factors that influenced on the response time include; the type of membraneand the presence of interferences which all slow the response time of these electrodes[(17)].

1.6.6 Stability and lifetime:

The stability and lifetime are features associated with the response behavior of ISEs. A number of problems affect the stability and lifetime of PVC based electrodes. They include the solution concentration, the interfering ions, which poison the electrode surface, the limited solubility of the active material, and its solvent, which affect the content of the membrane to leak away. All these lead to a positive or negative drift in the response and slope values, indicating that the electrode is approaching the end of its life [(18)].

1.6.7 Selectivity :

Ion selective electrodes are not entirely ion specific. This means that they may be sensitive to other ions to some extent in a system. In some situations where there are low ratio of interfering ion to the primary ion (ion of interest), interferences can be ignored. There are extreme cases

where the electrode may be far more sensitive to the interfering ion than to the primary ion and can only be used if the interfering ions are only present in trace quantities or completely absent. The interfering ion can be removed by chemical complexation or precipitation. The ability of an ion selective electrode to distinguish between different ions in same solution is expressed as the Selectivity Coefficient. The potentiometric selectivity coefficients are expressed according to the Nicolsky-Eisenman equation as:

$$\mathbf{E = E^0 + R\,T / Z_A F \ln [a_A + \Sigma K_{A,B} (a_B)^{Za/Zb}] \ldots\ldots 1.3}$$

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[19,20]. Potentiometric selectivity coefficients can be measured with different methods :

1.6.7.1 Mixed solution methods :

They are common and rapid methods for selectivity coefficient measuments[21]. K_{AB} can be evaluated by:

(a) Fixed Interference method (FIM) :

This is a situation where we have a constant activity of the interfering ion, a_B and varying activity of the primary ion, aA . The EMF values obtained are plotted against the logarithm of the activity of the primary ion. The intersection of the extrapolated linear portions of this plot indicates the value of a_A that is to be used to calculate K^{pot}_{AB} from the following equation:

$$\mathbf{K^{pot}_{AB} = a_A / a_B^{ZA/ZB}} \qquad \mathbf{\ldots\ldots\ldots 1\text{-}4}$$

Where, Z_A and Z_B have the same signs, positive or negative [22].

(b) Fixed primary ion method (FPM):

This is the opposite of the fixed interference method. There is constant activity of the ion of interest, a_A and varying activity of the interfering ion, a_B. The intersection of the extrapolated linear portions of this plot indicates the value of a_B that is to be used to calculate K^{pot}_{AB} from equation (1-4) [(22)]**.**

(c) Two solutions Method (TSM):

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 [(22)]:

$$K^{pot}_{A,B} = a_A(e^{\Delta EzA\ F\ /\ (R\ T)} - 1)\ /\ (a_B)^{\ Za/Zb} \quad \text{... 1-5}$$

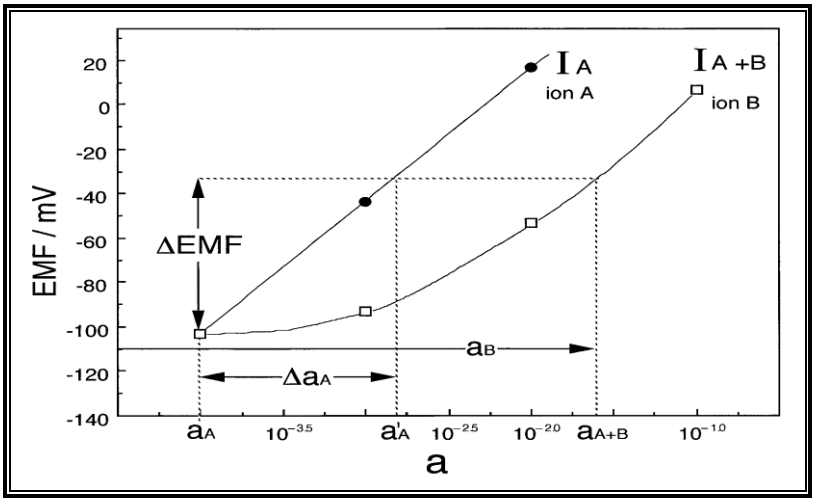
(d) Matched potential method (MPM):

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 ofthe primary ion A with a fixed activity is used as the referencesolution. The activity a_A is calculated from the ionic strength ofthe solution. While the primary ion is added step by step, thepotential change is measured and plotted against a_A (curve I_A) in Figure(1-4), another curve, I_{A+B}, is obtained from the potentialchange by stepwise adding the interfering ion B to the referencesolution with the same composition as on curve I_A.When thechange in potential (ΔE) on curve I_A at a'_A matches that oncurve I_{A+B}at a_{A+B}, the ratio between the activities of the primary ion A relative to the interferingion B denotes the selectivity coefficient $K^{pot}_{A,B}$.

The selectivity coefficient $K^{pot}_{A,B}$is thus obtained as [22,23] :

$$K^{pot}_{A,B} = \Delta a_A / a_B \quad \text{… 1-6}$$

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



Figure(1.4): Determination of selectivity coefficients by the matched potential method[22].

1.6.7.2 Separate solution methods:-

(a) When ($a_A = a_B$) :

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

$$\log K^{pot}A,B = (E_B - E_A)\, ZAF / R\,T \ln 10 + (1 - z_A/z_B) \log a_A \quad \text{…1-7}$$

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

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

Where (S) is the slope of the electrode.This method is recommended only ifthe electrode exhibitsa Nernstian response. It isless desirablebecause it does not represent as well the actual conditions under which the electrodes are used[24].

(b) When ($E_A = E_B$):-

The potential of an ISE for the primary and interfering ions are obtained independently. Then, the activities that correspond to the same electrodepotential value are used to determine the $K_{potA,B}$value and it equal [22]:

$$K_{pot}A,B = a_A / (a_B)\ Z_a/Z_b \qquad \ldots 1\text{-}9$$

1.7. Method of analysis:

1.7.1 Potentiometric measurement:

The method used depends upon many parameters such as the analyse and the required accuracy and precision for such analyses. These methods are grouped into direct reading, standard addition and potentiometric titrations.

A- Direct potentiometric methods :

This is the simplest and most widely used method of obtaining quantitative result using ion-selective electrodes. A calibration graph is constructed by measuring the equilibrium cell potential for several solutions of known concentrations. Then the potential of the sample is measured at the same conditions, and the concentration is read directly from the graph. This method is extremely rapid, enabling measurements to be complete in two or three minutes. This method is suitable for the analyses of all samples in which the analyte of interest is present in the free un complexed states [25].

B- Standard addition method (single point):

This method is generally more accurate than direct method for concentration, but it is more time-consuming because of the calibration involved . The electrode potential of a known volume of unknown solution is measured and small volume of a known solution is added to the first volume and the electrode potential re-measured, from which the potential difference ΔE is found. By solving the following equation the unknown concentration can be obtained[25]:

$$Cu = Cs/10^{\Delta E/s(1+Vu/Vs)-(Vu/Vs)} \qquad \ldots\ldots\ldots\ldots 1.10$$

Where Cu: the concentration of unknown solution
Cs: the concentration of standard solution
Vu: the volume of unknown solution
Vs: the volume of standard solution
S: the slope of electrode.

C- Multiple standard addition:

In this method several addition of standard solution to the same Sample to be measured in order to increase the accuracy and decreases the error. It is an extension of standard addition.The response of (ISEs) to certain analyte A in solution free from interfering ions can be represented by Nernstain equation:

$$E=E_0 +S \log (C+X\ Vs/Vu) \qquad \text{……..1.11}$$

Where: S: slope
Vs: volume of standard addition.
Vu: volume of unknown.
C: concentration of unknown.
X: concentration of standard addition .

Vu is usually set to be hundred times more than Vs. Rearranging of equation and taking the antilog gives:

Antilog (E/S) = constant (C+X Vs/Vu)

Where antilog (E/S) is constant thus the antilog (E/S) is proportional to V_s[26]. A plot of antilog (E/S) against Vs, a straight line is obtained, the intercept of which with the volume axis denote the end point of the unknown concentration in an addition method.

D- Gran's plot :

Is a way of linearizing the data obtained in potentiometric titration and thus easily and precisely locating the equivalence points of titrations.The plots are used in work with ISEs, for this original purpose and also for linearizing data from multiple standard addition procedures. The technique may be applied to both complexometric and precipitation titrations[27].

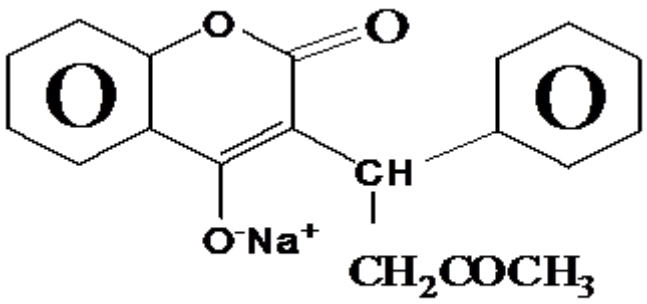
1.7.2 Potentiometric titration :

This method can increase the precision of ISE measurements and alsothe number of ionic species that can be determined. ISEs are commonly used as indicators for the titrant or sample species to follow the progress of a precipitation or complexation titration. A small change in reactant addition corresponds to a large change in electrode potential at the stoichiometric end point. The sample is titrated with a suitable titrant and the increase or decrease in titrant activity is followed with an ion-selective electrode response, to locate the equivalence point.

A direct plot of potential as a function of titrant volume, the midpoint in the steeply rising portion of the curve is estimated visually and taken as end point. A second approach to end point detection is to calculate the change in potential per unit volume of titrant $\Delta E/\Delta V$ plotted versus the average volume of titrant, the maximum is the end point [12,28].

1.8 Warfarin sodium

Warfarin sodium 3-(α -acetonyl benzyl)4-hydroxy coumarin sodium salt is an anticoagulant, used in prevention and treatment of venous thromboembolism[29,30]. Presence of coumarin ring makes Warfarin a good complexing ligand. Coumarin complexes are of significant interest because of their biological [31] and complexing ability[32,33]. The chemical formula of warfarin sodium is $C_{19}H_{15}NaO_4$, and its structural formula show by the following Figure :



Figure(1.5) : Structur of warfarin sodium

Crystalline warfarin sodium occurs as a white, odorless, crystalline powder, is discolored by light and is very soluble in water; freely soluble in alcohol; very slightly soluble in chloroform and in ether [34]. The sodium salt of warfarin has become the most widely used in order to improve the physicochemical properties of warfarin such as solubility, dissolution rate, hygroscopicity, chemical stability, crystal form and mechanical properties [35].

Warfarin is an anticoagulant drug, which competitively depresses the synthesis of vitamin K-dependent coagulation factors [36].

Warfarin inhibits the action of vitamin K epoxide reductase, whose gene (VKORC1) was discovered in 2004 by two independent teams[37,38]. Another key factor influencing warfarin bioavailability is its transport in blood, where some 99% is found bound to the Sudlow binding sites of human serum albumin (HSAa).[39]

Currently, the anticoagulant effect of warfarin is indirectly measured through the correlation of the clotting time (prothrombin time) and the amount of the drug present in blood[40] .

The compound was first synthesized by Schroeder and Link [41] with two solid forms available-amorphous and crystalline clathrate. The amorphous form isstable in ambient conditions. The crystalline clathrate form is warfarin sodium-isopropyl alcohol complex, which is prepared either from warfarin or amorphous warfarin sodium to eliminate impurities in warfarin sodium [42] .

In an attempt to decrease the toxicity of warfarin induction,several clinical dosing algorithms have been proposed [43,44], but none has been well accepted. A major barrier to their use is that they were developed for middle-aged inpatients who could tolerate doses of 5–10 mg warfarin dailyand who had daily monitoring of the INR. Today,the typical person taking warfarin is elderly.Because warfarin dose requirements decrease with age ,use of existing algorithms tends to overdose the elderly [45,46].

The most analytical methods havebeen reported for determine warfarin such as high performance liquid chromatography (HPLC)with fluorescence detection [47,48], LC and HPLC with UV detection[49,50], HPLC-MS/MS [51,52], multi-mode UPLC (ultra performanceliquid

chromatography)-MS/MS method [53,54]LC-MS/MS [55],chiral capillary electrophoresis with spectrophotometric detection [56], chiral stationary-phase liquid chromatography-fluorescencesystem coupled with on-line circular dichroism detector [57] andtime-correlated single-photon counting [58]. However, there maybe several disadvantages for these methods. For example some ofthem are time consuming and tedious, while others use large bio-logical fluid volumes and need expensive instruments and toxicsolvents, plus time consuming procedures. And there are several methods havebeen reported for quantification of warfarin in biological samplesare: HPLC with detector of UV–vis [59,60] ,HPLC with detector of fluorescence [61,62], gas chromatography with detector of mass[63], differential pulse and/or square-wave stripping voltamme-ters [64,65], fluorescence spectrophotometry[66,67], and capillaryzone electrophoresis with detector of PDA [68,69] .In all of these methods, the biological sample preparation.

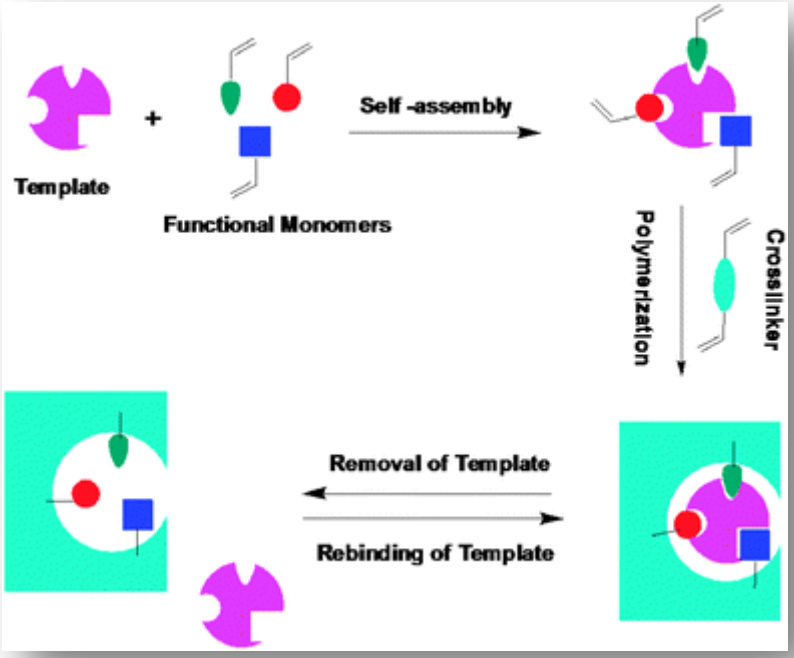
1.9 Molecular Imprinted Polymer:

Molecular imprinting is a process in which functional and cross-linking monomers are copolymerized in the presence of the target analyte (the imprint molecule), which acts as a molecular template. The functional monomers initially form a complex with the imprint molecule. After polymerization, their functional groups are held in position by the highly cross-linked polymeric structure [70,71] as illustrated in Figure (1.6). Additionally, the steric arrangement of these interactions around a given substrate, molecular template, is a crucial aspect necessary for the creation of binding pockets providing complementary size, shape, and functionality for preferentially facilitating selective recognition along with a high affinity toward the target. Thus, the recognition process in MIPs may be described in analogy with mechanisms established for enzyme– substrate-complexes such as, for example, the lock-and-key. [72]

Molecular imprinting can also be defined as a method for creating specific cavities in synthetic polymer matrices with memory for the template molecules[73].

Those materials are physically stable, resistant to mechanical stress, high pressure and elevated temperatures. Furthermore, MIPs possess an imprint memory of more than 100 times without loss of memory. These characteristics made a MIP an ideal analytical material.

The synthesis of MIPs usually involves a parallel process involving synthesis of a non-imprinted polymer (NIP) under conditions identical to those of the MIP except that the template is absent. In principle, the NIP is entirely analogous to the MIP except that any binding sites within its porous structure are non-selective. The NIP can therefore be used as a benchmark for assessing the selectivity of the MIP such as recovery and breakthrough as reported in published papers. (74)



Figure(1.6): Representation of the principle of molecular imprinting(74).

1.10 Approaches for Preparing Molecularly Imprinted Polymers

The main techniques for generating MIP can be divided into two groups, namely, covalent and non-covalent, on the basis of the type of binding between the template molecule and the functional groups of the monomers in the prepolymerization step. Other derivatives of these

approaches, especially semi-covalent or metal-mediated imprinting, have been applied to organic MIP preparation.

1.10.1 Covalent Imprinting Method: This technique, also known as the preorganised approach, consists of the reaction of the template molecule with polymerisable monomers by reversible binding.
Polymerisation takes place in the presence of a large excess of cross-linker to yield an insoluble rigid network. The covalent bonds have to be cleaved for template extraction, leading to defined binding sites of complementary steric and functional topography to the template molecule. Reversible cleavage and formation of the covalent bonds are the basis of molecular recognition. [75,76,77]

1.10.2 Non-Covalent Imprinting Method: This method, also known as the self-assembly approach , is inspired by nature where non-covalent interactions play a key role in molecular recognition processes, and is accepted as the most successful and commonly applied method for MIP synthesis .
The prepolymerization complex between the template molecule and the functional monomer is stabilised by weak interactions including electrostatic (charge-charge) interactions, dipole interactions, London dispersion or hydrogen bonding, which will also govern the rebinding process. [75,76,77]

1.10.3 Semi-Covalent Imprinting Method: In this procedure, the template is covalently bound to a polymerisable group for polymer synthesis, but template rebinding takes place via non-covalent interactions. After polymerisation with an excess of crosslinker, the resulting network was hydrolysed to release the template molecule. In general, this approach combines the advantages and limitations of the covalent and non-covalent imprinting[78,79,80].

1.11 Molecular Imprinted Polymers Components and Factors Influencing Polymerization:

As described previously, the basic components required for the synthesis of an MIP consist of the template molecule, one or more functional monomers, a cross-linker, a polymerisation initiator and a solvent.

1.11.1 Template Molecule: Various substances can act as the template molecules in the molecular imprinting technique. For example, carbohydrates, amino acids and their derivatives, organic amines, vitamins, proteins, and other molecules have been successfully used as template molecules in the preparation of MIPs. Typically, these molecules contain highly polar groups (such as carboxyl and amino). It is easy to prepare high-performance MIPs because strong polar groups and the functional monomer could form more stable molecular complexes. The molecular imprinted polymers with high selectivity and affinity can be produced from the imprinted molecules that can form hydrogen bonds with the functional monomer, due to the outstanding advantages of hydrogen bonds in terms of its directionality, saturation and strength. Macromolecules, supramolecular cells, and even metal ions are also used as the template molecule. [75]

1.11.2 Functional Monomer: The functional monomer provides the functional groups which are responsible for the binding interactions with the target molecule in the imprinted cavities. Thereby, as described previously, stronger interactions between the template and the functional monomer during imprinting, result in MIP with higher binding capacity and selectivity. In some cases, monomer reactivity can be affected by complex formation with the template molecule . Functional monomer can provide specific functional groups in polymerization or copolymerization.

In various polymerization reaction the most widely used one is free radical polymerization. During the polymerization process, the molar ratio of imprinted molecule and functional monomer has a great effect on the generation of the specific cavities.

Generally, with the ratio of functional monomer to the template molecule increasing, one can make the self-assembly of template molecule to functional monomer easy and fully complete on the one hand it will do harm to the polymerization for the high ratio of proportion of functional monomer, since the excess of functional monomer leads to an increase in non-selective binding sites generated by non-assembled functional monomer residues in the polymer. On other hand, excess functional monomer may cause self-aggregation, which result in reducing selective binding sites. The mole ratio of template molecule to functional monomer are generally controlled as 1:4. In additional functional groups of the

imprinted molecules and the properties of solvent should also be considered during the preparation.[75,81]

1.11.3 Cross-linker : Cross-linkers bridge the linear molecules so as to bond with each other among molecules to establish a network, and they also promote or regulate the polymer chain formation. The cross-linker in the synthesis of molecular imprinted polymers acts in three aspects:

(a) They control the morphology of MIPs.
(b) They fix imprinted recognition sites.
(c) They affect the mechanical stability of the MIP array. [75]

The amount of cross-linker directly affects the number and the cross-linking degree of active functional monomers in the unit mass of imprinted polymer, whereas the number of active functional monomer and cross-linking degree directly influences the selectivity of MIPs and the binding capacity.
In conclusion, the ratio of functional monomer to cross-linker has a great impact on the properties of molecularly imprinted polymers. When the amount of cross-linker is less, the cavity configuration of MIPs cannot maintain itself in a stable state due to insufficient cross-linking. However, an excess of cross-linker decrease the number of functional monomer in unit mass and then reduced the number of recognized sites.[75,82).

1.11.4 .Initiator: Most MIPs are synthesized using free radical polymerization (FRP), either thermally or photochemically induced. The process consists of three basic steps: initiation, propagation and termination.
In the first step, radical generation is usually accomplished by the decomposition of an initiator; increasing the concentration of the initiator results in higher polymerization rates, but lower polymer molecular weights. The most important initiators used in FRP are azo compounds, peroxo compounds, redox systems and photo-initiators. The generation of free radical from azo initators can be accomplished either by UV-irradiation, at the maximum absorption wavelength of the compound, or by heating at its decomposition temperature.[77,83]

1.11.5 Solvent : Play important role in the imprinting process . Poreforming solvents, referred to as porogens, are applied during imprinting with The ultimate goal of obtaining macroporous polymeric network to facilitated mass transfer and allow easy access of the analyte to the binding sites.

The solvent serve to bring all the components of the polymerization (monomer, template, initiator and cross-linker)into one phase and has significant effect on the texture (pore size distribution and shape)and physical form of synthesized material and promote the bonding of the guest molecules.[77,82]

1.12. Aim of the work:

This project was to construct and characterize several types of ion-selective electrode for the potentiometric determination of warfarin sodium in pure and pharmaceuticals :

A) The first type included fabrication of membranes for warfarin sodium (WFN) was constructed by warfarin sodium with Dodeca-molybdo phosphoric acid (MPA), Dodeca-phosphotungstic acid (PTA),and many plasticizer : oleic acid (OA), tri-n-butyl phosphate(TBP), Nitrobenzene (NB), Acetophenone (AP) and di-octyl phthalate (DOPH) in PVC matrix membrane . The constructed electrodes characteristic parameters that include slope ,liner range , detection limit, lifetime, selectivity, and working pH range will be investigated. Also, the statistical treatments were applied for the analytical results.

B) The second type included fabrication of membranes by using molecularly imprinted polymer , The study involves the preparation of MIPs and NIPs for the warfarin sodium (WFN) as templates using two kinds of functionl monomers, Methacrylic acid (MAA) as acidic monomer and Acrylamide (ACY) as basic monomer,and study the characteristic parameters that include slope, linear range, detection limit, lifetime , selectivity, and working pH range for these electrode.

2- Experimental part

2.1. Instruments and equipment's:

1-A digital pH/ion meter (inoLab 740 with terminal 740 – WTW,Germany).

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

3- Infrared spectrophotometer SHIMADZU, FTIR-8000 (Japan).

4- Expandable ion analyzer, HANA(Italic), model pH meter 211.

5- Reference electrode single junction, ORION, model 90-01 Saturated calomel electrode (SCE) .

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

7- Silver-silver chloride wire.

8- PVC tubing (6 mm i.d.).

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

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

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

12-Nitrogen gas system.

13-Scaning Electron Microscopy (Inspect S50) Nether land (Tokyo, japan).

14- Laboratery oven .

15- vacum desicator (Barnant company) .

2.2-Chemicals:-

1- Warfarin sodium standard ($C_{19}H_{15}NaO_4$ M.W 330.31 g mol^{-1}) was a gift from the State Company of Drug Industries and Medical Appliances (SamaraIRAQ-SDI).

2- Commerical drugs: warfarin 1mg (Bristal) (UK),warfarin 3mg (Actavi) (UK), Orfarin (3mg) Finland .

3- Dodeca-molybdo phosphoric acid (MPA) ($H_3PO_4.12MoO_3.24H_2O$; M.W. 2257.6), (Analar, 99.6%).

4- Dodeca–Phosphotungstic acid (PTA) ($H_3PO_4.12WO_3.XH_2O$; M.W. 2880.21), (Analar, 99.3%).

5- Methacrylic acid (2-methyl propeonic acid),($C_4H_6O_2$. M.wt . 86.09 g mol^{-1}),(sigma-aldrich 99%).

6- Benzoyl peroxide ($C_{14}H_{10}O_4$. M. wt. 242.23),(78% Sigma-Aldrich).

7- Ethylene glycol dimethacrylate ($C_{10}H_{14}O_4$. M.wt. 198.22 g mol^{-1}), (98% Sigma-Aldrich).

8. Acrylamide (C_3H_5NO M. wt. 71.08 g·mol^{-1}) , (99% BDH).

9- Chloroform ($CHCl_3$ M. wt. 119.38 g. mol^{-1}), (99.7% Analar).

10- Tetrahydrofuran (C_4H_8O; 72.11 g mol^{-1}), (Fluka AG, 99.5%).

11-Polyvinyl chloride (PVC) of relatively high molecular weight (Fluka AG, 98%).

12- The plasticizers were obtained from Fluka AG, (Switzerland), their composition and viscosities are tabulating in Table (2.1).

13- Other chemicals: hydrochloric acid (HCl; 36.45 g mol^{-1} sp.gr. 1.184; 37% HCl; 12M), ammonium hydroxide (NH_4OH; 35.05 g mol^{-1} sp.gr. 0.90; 28% NH_3; 14.82M), sodium chloride (NaCl; 58.44 g mol^{-1}) , potassium chloride (KCl; 74.55 g mol^{-1}) , aluminum (III) nitrate ($Al(NO_3)_3.9H_2O$; 375.13 g mol^{-1}), iron(III) nitrate [$Fe(NO_3)_3.9H_2O$; (404.02 g mol^{-1})], magnesium chloride ($MgCl_2$; 95.21 g mol^{-1}), calcium chloride ($CaCl_2$; 110.98 g mol^{-1}) ,Alanine ($C_3H_7NO_2$; 89.09 g mol^{-1}),serine ($C_3H_7NO_2$;105.09 g mol^{-1}) ,proline ($C_5H_9NO_2$;115.13 g

mol^{-1}), All chemicals and solvents were of analytical reagent grade obtained from BDH, Fluka and Aldrich companies. Distilled water was used throughout the study.

Table (2.1): Shows the plasticizer which were used and their chemical composition

Plasticizer's name	Chemical composition	Viscosity	company
Nitrobenzene (NB)	$C_6H_5NO_2$	2.030 cST	Fluka
Acetophenoe (AP)	C_8H_8O	1.64 cST	Fluka
Di-octylphthalate (DOPH)	$C_6H_4[CO_2C_8H_{17}]_2$	82.98 cST	Fluka
Tri-butylphosphate (TBP)	$C_{12}H_{27}O_4P$	3.114 cST	Fluka
Oleic acid (OA)	$C_{18}H_{34}O_2$	39.2 cST	Fluka
Tritolyl phosphate (TP)	$C_{21}H_{21}O_4P$	65-75 cST	Sigma Aldrich
Dibutyl sebacate (DBS)	$C_{18}H_{34}O_4$	6.11 cST	Sigma Aldrich

2.3. Preparation of Stock Solutions:

1- The stock standard solution of 0.1 M warfarin sodium was prepared by dissolving 1.6516 g in 50 ml of distilled water . More diluted solutions ranged from 10^{-6} – 10^{-2} M were prepared by subsequent dilution of the stock solution.

2-The stock standard solution of 0.01 M Dodeca- molybdo Phosphoric acid and Dodeca- phospho tungestic acid were prepared by dissolving (1.1288 g) and (1.4401 g) respectively in 50 ml of distilled water .

3- 0.1 M stock solution of each of interfering salt KCl , NaCl ,$CaCl_2$, $MgCl_2$, $Fe(NO_3)_3.9H_2O$, $Al(NO_3)_3.9H_2O$, were prepared by dissolving of (0.3725 g ,0.2925 g , 0.5541 g , 0.4760 g , 2.0201 g and 1.8750 g) respectively in 50

ml of distilled water . More diluted solutions ranged from (10^{-6} – 10^{-2}) M were prepared by subsequent dilution of the stock solution.

4- 0.1 M stock solution of each of interfering amino acid alanin, proline, serine were prepared by dissolving of (0.4455 g ,0.5757 g and 0.5255 g) respectively in 50 ml of distilled water. . More diluted solution ranged from (10^{-6} – 10^{-2}) M were prepared by subsequent dilution of the stock solution .

2.4. Preparation of Ion-Pair Complex:

The preparation of ion-pair (WFN-MPA) and (WFN-PTA) was prepared by mixing 50 mL of 0.01 M solution of warfarin sodium (WFN) with 50 mL of 0.01 M solution of molybdo phosphoric acid (MPA) with phosphotungstic acid (PTA) with stirring. The resulting are white precipitates formed after 24 hr, filtered, washed with water, dried at room temperature for two days using the vacuum desiccator.

The composition of the two ion-pair compounds (WFN-MPA) and (WFN-PTA) were confirmed using infrared spectroscopy (FTIR).

2.5. Preparation of warfarin sodium electrodes:-

2.5.1. Composition of membrane:-

Ten warfarin sodium ion-selective electrodes were prepared depending on the use of ion-pair compounds warfarin sodium- molybdo Phosphoric acid and warfarin sodium-phosphotungstic acid (PTA)as the electro-active substances with five plasticizers (OA, TBP, NB, DOPH, AP).

The method that followed for immobilization of the ion-pair compounds into the PVC matrix membrane as described by Craggs et al [(84)]. 0.040 g of electro-active precipitates was mixed with 0.360 g of plasticizer and 0.170 g of PVC powder; all were dissolved in 5-6 mL of THF with stirring until a clear viscous solution was obtained.

2.5.2. Assembling the ion-selective electrode:

Each of the above solution was poured into a glass casting assembly which It consists of two pieces; a glass cylinder (30mm height and 35mm diameter),mounted on a glass plate The two pieces were pasted together via a (PVC-THF) viscous mixture (to make sure for 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 (~200 g) 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 plate as shown in Figure (2.1). 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, one of the sides of PVC tubing was flatten out and smoothed by vertical rotation on a glass plate moistend with THF-PVC solution.

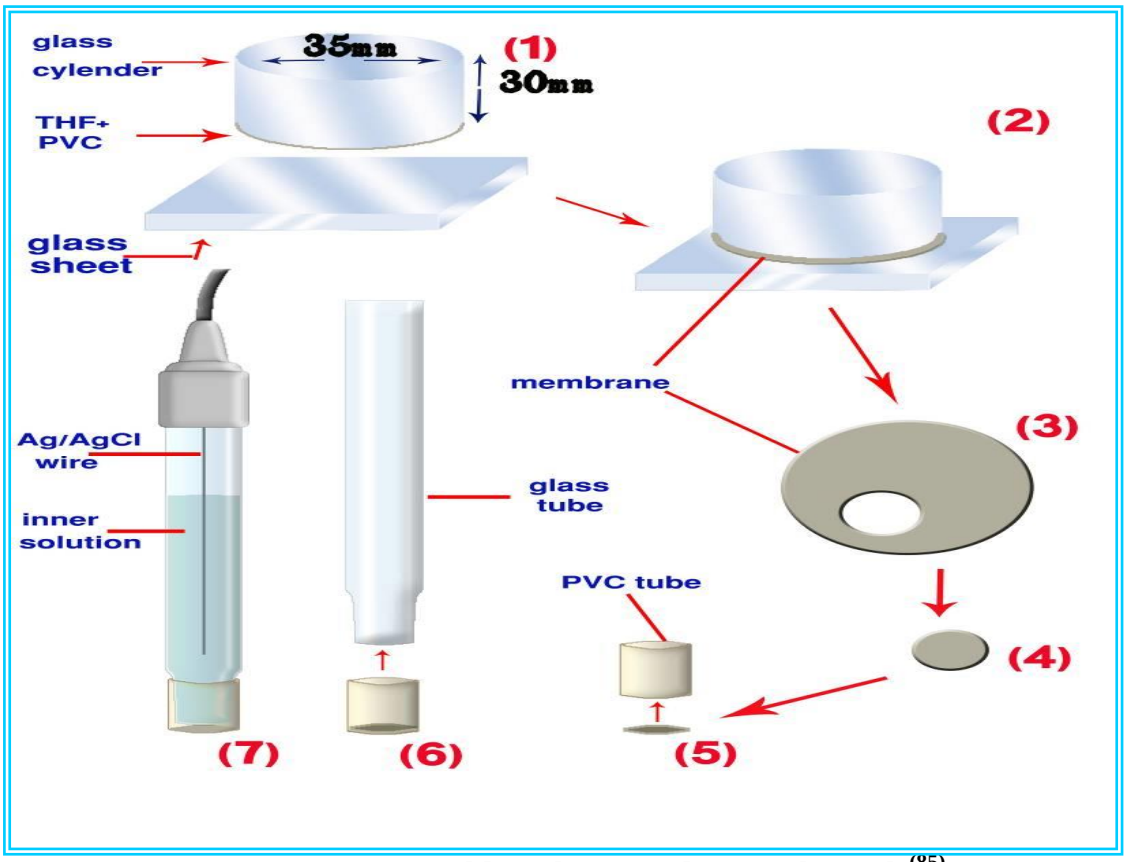


Figure (2.1): Assembling the Ion-Selective Electrode[(85)].

The membrane disc then mounted with a forceps on the polished end and the outer edge of the disc membrane was carefully sealed to the end of the PVC tube. The next step is the connection of the PVC tubing to one side of 10cm glass tube .The other side of the glass tube was assembled with plastic cover in which Ag/ AgCl wire was inserted through. The tube was filled 3/4 with 0.1 M warfarin sodium solution before fixing the cover.

The electrode was then conditioned by placing it in 0.1M solution containing the drug to be measured (at least for 2hour's) before using.

2.6. Potential measurement

Warfarin sodium selective electrode and saturated calomel electrode (SCE) were used as indicator electrode and reference electrode, respectively. The e.m.f. measurements were carried out at room temperature using the following cell:

SCE. | test solution | ISEs

A calibration curve was constructed for each ISEs using several standard solutions ranged from (10^{-6} – 10^{-1})M warfarin sodium . The test solutions were constantly stirred during measurements with magnetic stirrer. Calibration curves were prepared by plotting the potential versus the concentration on Orion 7 cycle semi-logarithmic graph paper (manual calculation E versus log c.). From the calibration curve, all the characteristic parameters of the ISEs were obtained including slope, correlation coefficient, concentration range 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 1-12 obtained by addition of small volumes of hydrochloric acid and/or ammonium hydroxide solutions. The life time of each membrane was calculated, by monitoring the decrease in response with the time.

2.7 Selectivity measurements:

The selectivity of the studied electrodes were measured by two methods:

1-The separated solution method (SSM) : In this method, standard solutions (10^{-6} – 10^{-1}) M warfarin sodium were prepared and their potentials were measured. At the same time the potential for interfering species (K^+, Na^+, Ca^{2+}, Mg^{2+}, Al^{3+}, Fe^{3+}, alanin, proline and serine) which were selected due to their biological importance at concentrations range from (10^{-6} – 10^{-1}) M, were measured. From equation (1-8), the selectivity coefficient can be calculated.

2- Match potential method (MPM), this method involes the using one standard solution of warfarin sodium with concentration of 10^{-3} M in 50 mL

then aliquot 10 mL of standard solution and added 0.1 mL of 0.1 M from standard solution of warfarin sodium which has concentration 100 times than that of sample, and measured the potential of standard solution 10^{-3}M before and after each addition of standard solution.The same concentration 10^{-3}M aliquot 10 mL added 0.1 mL of 0.1M of interfering species (K^{+},Ca^{2+},AL^{3+}, alanin, proline and serine). Measured potential before and after each addition of interfering species but the potential for standard solution 10^{-3}M are same for two aliquots because the same of concentration. The potential response to interfering ions was then measured according to equation (1-6).

2.8. Standard analysis:

Two synthetic samples of warfarin sodium in the concentration of 10^{-3}, 10^{-4} M were prepared. The concentration of these samples were calculated using direct, standard addition (SAM) and titration method .

In the direct method the e.m.f. of sample is measured directly using warfarin sodium indicator electrode .The concentration was then calculated using calibration curves.

In the standard addition method;to 10 mL sample solution with concentration of (10^{-3}-10^{-4} M) successive amounts, is introduced five additions of 0.1 mL of 0.1M increments of warfarin sodium solution were added . The e.m.f. is measured before and after each addition. The concentration of the sample is calculated using equation (1-10) for a single point increment. This method depends on the fact that the plot of electrode potential (mV) against concentration (M) is a logarithmic curve. Thus any particular ratio of the amount of increase in mV in response to a particular increase in concentration (i.e. the slope of the curve) will only fit in one unique part of the curve and thus the concentration before and after addition can be determined.

A precipitation titration was then performed for the potentiometric determination of warfarin sodium samples. In this method, a 10 mL sample solutions containing warfarin sodium with concentration of 10^{-3},10^{-4} M were titrated against $10^{-3}$and 10^{-4}M of each of dodeca molybdo Phosphoric acid and Dodeca Phosphotungstic acid solution. Potential was measured after each addition using the prepared ISEs.

2.9. Preparation of pharmaceutical samples

Three types of tablets were used to determined warfarin sodium :

1. Bristol 1 mg of warfarin sodium (UK).

2. Actavis 3 mg of warfarin sodium (UK) .

3. Orfarin 3 mg of warfarin sodium (Finland) .

A total of 14 tablets of warfarin sodium were grinded and weighed. Accurately weighted and powdered. An aliquot of powder equivalent to the weight of 1 tablet was accurately weighed and transferred to volumetric flask and was dissolved in 100 ml of distilled water stirring for about 30 min. This solution was filtered to remove any insoluble matter. The filtrate was collected in a clean flask.

2.10. Synthesis of the Moleculary Imprinted Polymers (MIP):

In 25 mL screw cap glass test tube, 3 mmol of monomer (methacrylic acid or acrylamide), 15 mmol of the cross-linker (Ethylene Glycol DiMethyl acrylate) EGDMA,0.5 mmol of warfarin sodium (WFN), 0.3 mmol of benzoyl peroxide (BPO) as initiator and 4mL of chloroform were mixed. The solution was degased for 30 minutes with high purity nitrogen and cured at 60 ^{o}C for 20 minutes. The polymer was dried , crushed and the template was removed by repeated washing with (30 %) acetic acid via soxhlet extraction. The polymer was dried at 45 ^{o}C for 24 hours. The polymer was then ground, sieved and particles with size less than 150 μm was collected and used for preparing the sensing membrane. The non-printed polymer was (NIP) was made in the same way but without the template drug.[86]

2.11.Synthesis of Membrane and Electrode Construction

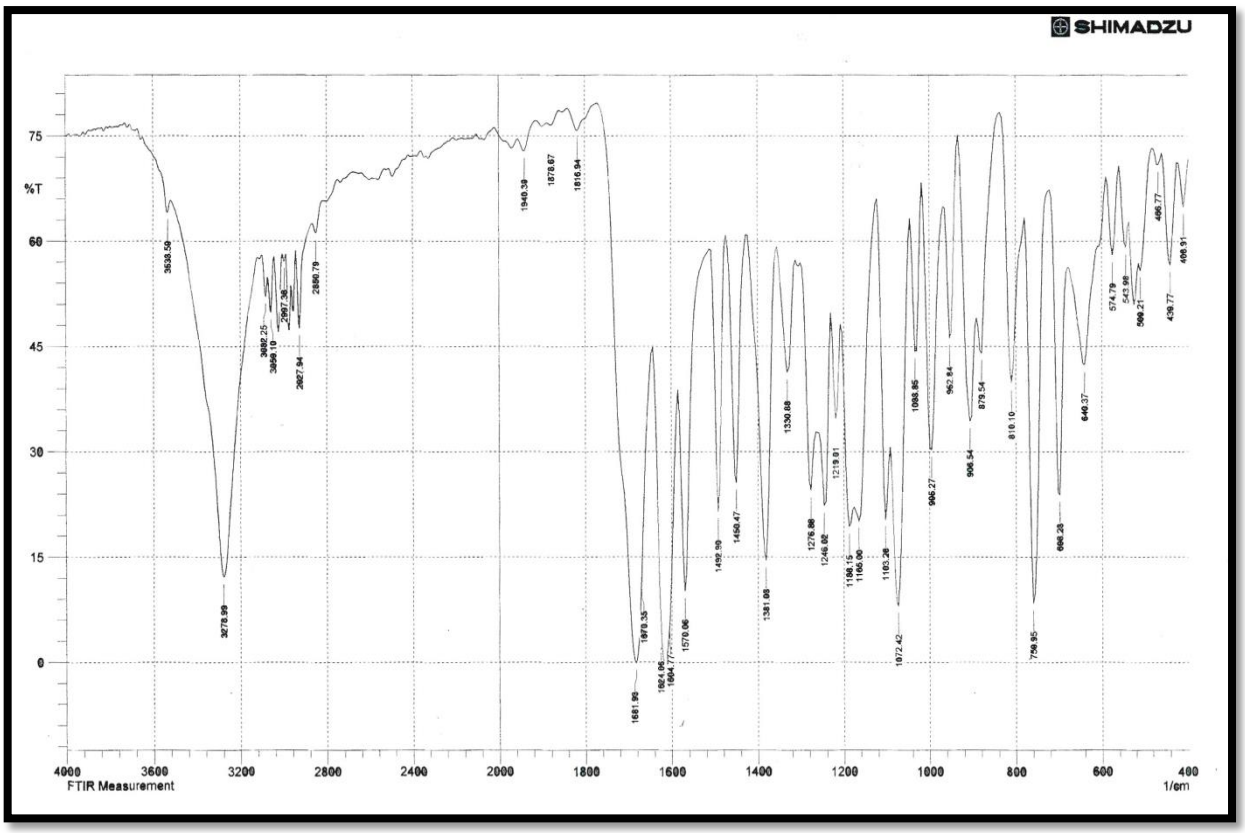
The sensing PVC membrane was prepared by mixing 0.170 g of PVC, 0.400 g of the plasticizer (TP , DBS) and 0.020 g of the MIP. After homogenization, 4-5 mL of THF was added and stirred. The mixture was pour into a glass cylinder (30mm height and 35mm diameter) and allowed to evaporate for 2 day . The electrode was made in the sam as of Figure (2-1). The electrodes were preconditioned by soaking for two hours in 0.1 M solution prior to use[84].

3.1. Warfarin sodium Ion Selective Electrodes:

In this study ten new ionphores as potentiometric sensors for warfarin sodium were prepared using dodeca-molybdo phosphoric acid and dodeca phosphotungestic acid, as an ion-paring agents. Association complexes for sparingly soluble white complexes of warfarin sodium with dodeca-molybdo phosphoric acid(WFN-MPA) and dodeca phosphotungestic acid (WFN-PTA) as counter an ions, were instantaneously formed upon the addition of dodeca-molybdo phosphoric acid or dodeca phosphotungestic acid to warfarin sodium solution . The dry powder of the ion pair (WFN-MPA) and (WFN-PTA) were used to construct ten warfarin sodium electrodes. The electro-active compounds (WFN-MPA) and (WFM-PTA) were confirmed using FTIR. Figure (3.1),(3.2)and(3.3) show the spectra of warfarin sodium and the two (WFN-MPA),(WFN-PTA) complexes, respectively. The coordination sites of the warfarin sodium involved in the bonding with molybdo Phosphoric acid (MPA) and phosphotungestic acid had been determined by careful comparison of the FIR spectra of the complexes with that of the parent drug. The full spectrum of the drug is highly complicated only diagnostic those bands of coordination with metal ions have been considered for discussion. These bands were tabulated in Table (3.1).

Table (3.1): Structural important FTIR bands of warfarin sodium and their Complexes (WFN-MPA) and (WFN-PTA) .

Assignment	WFN	WFN-MPA	WFN-PTA
OH str.	3278	3556	3280
C-H aromatic	3082,3059	3001	3022
C-H aliphatic	2850	2881	2929
C=O str.	1681	1720	1711
C=C str.	1604	1608	1616
CH bending aliphatic	1492,1450	1454	1452
C-O str. Asymm	1276	1265	1276
C-O str. Symm	1165	1161	1103
Out-of plane-mono-sub	759	759	759



Figure(3.1): FTIR spectrum of standard warfarin sodium.

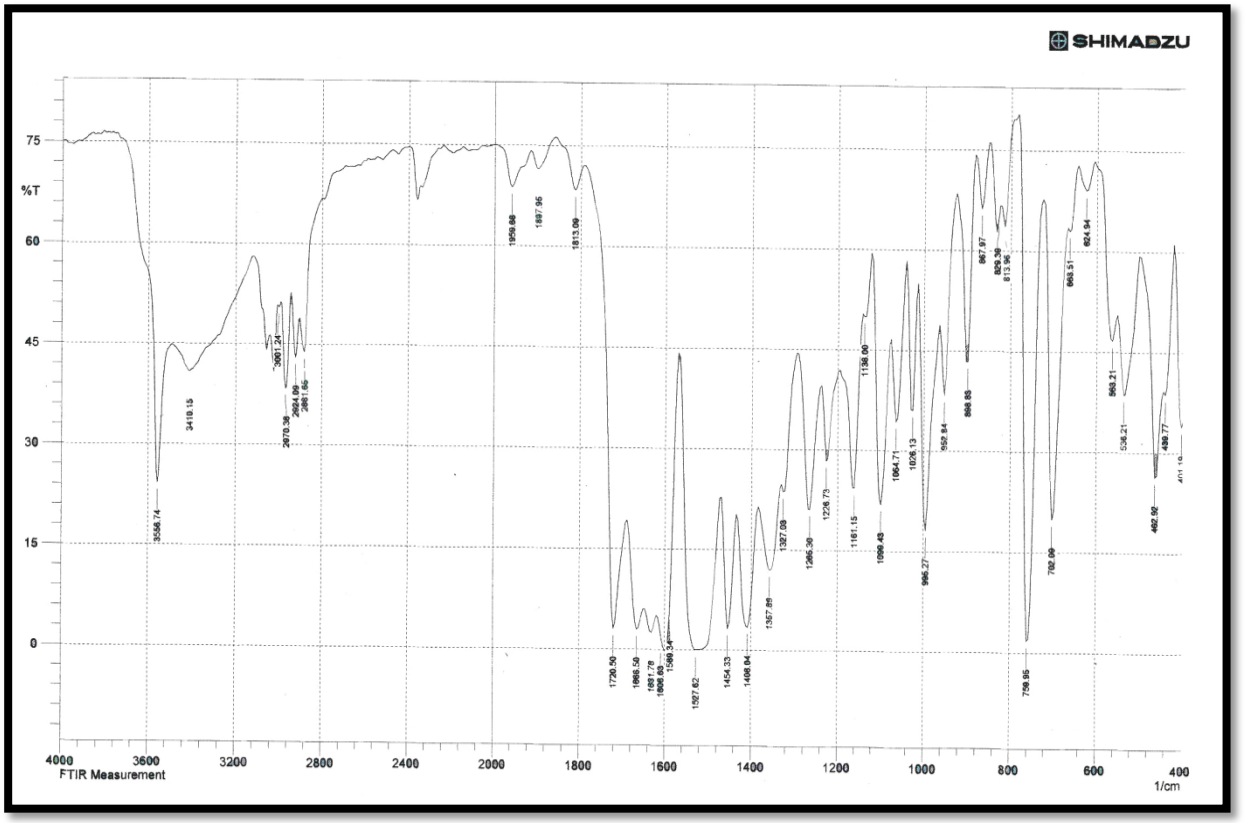


Fig. (3.2): FTIR spectrum of warfarin – MPA complex.

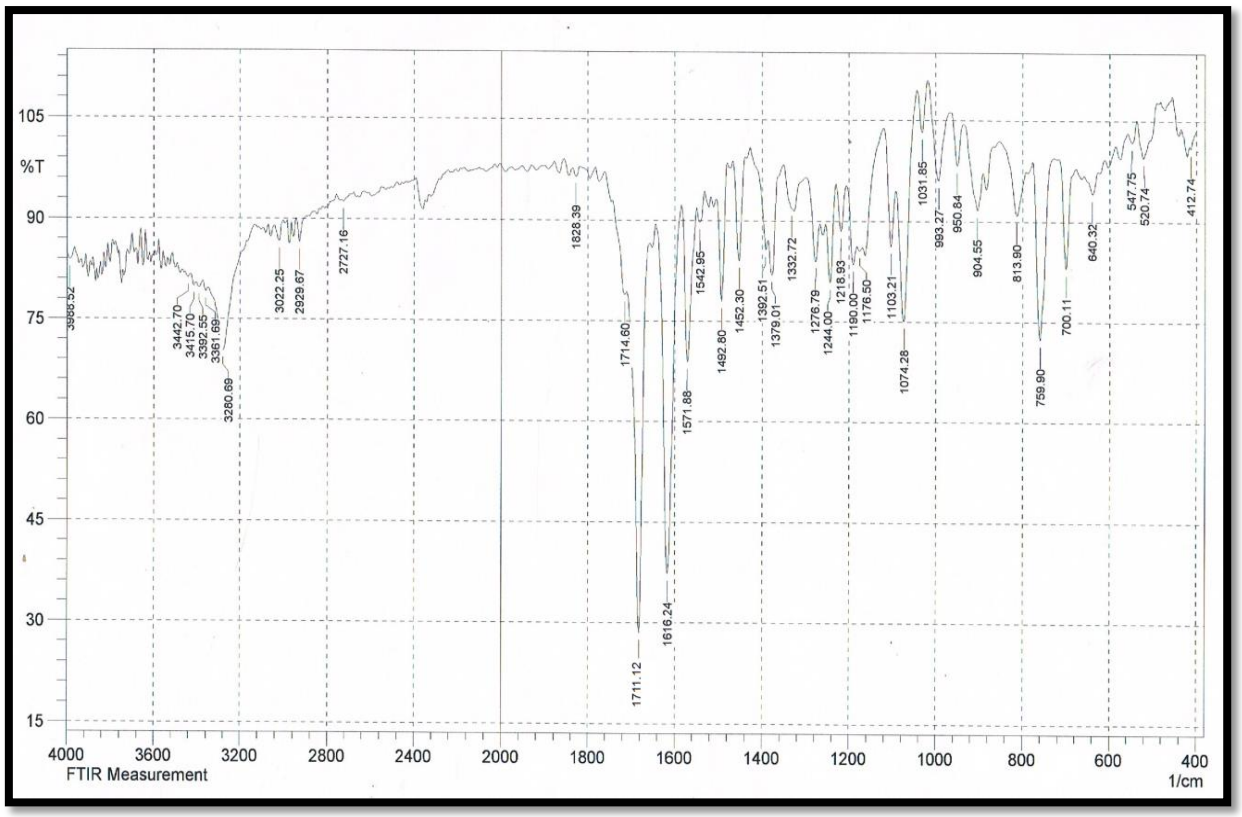


Figure (3.3): FTIR spectrum of warfarin – PTA complex.

3.2. Sensor Characteristics of warfarin sodium :

The potentiometric response characters of sensors which are based on warfarin sodium– molybdo Phosphoric acid (WFN-MPA) and warfarin sodium- phosphotungestic acid (WFN-PTA) ion-pair complexes as the electro-active materials and five plasticizers: Oleic acid (OA), tri-butylphosphate (TBP) ,Nitro benzene (NB), Acetophenone (AP) and di-octyl phthalate (DOPH) in PVC matrix, were examined. The effect of different plasticizers were studied with respect to the slope, response time, linear concentration range, life time, limit of detection and working pH range. The potential values of these electrodes were plotted versus the logarithm of concentration of drug. All membranes were soaked in 1×10^{-1} M drug solutions for two hours in order to condition the membrane before determination.

3.3. Warfarin sodium ISEs :

3.3.1. (WFN-MPA ,WFN-PTA+OA) :

Membranes based on Oleic Acid (OA) as a plasticizer was measured at different concentrations of warfarin sodium range from (10^{-6} - 10^{-1}) M. calibration plots are shown in Figure (3.4) :

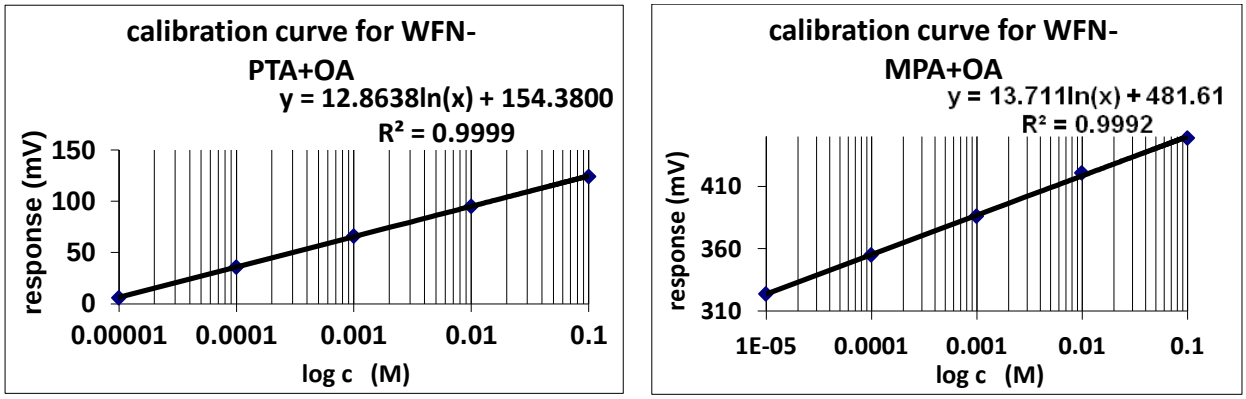


Figure (3.4): Calibration curve of WFN-MPA , WFN-PTA selective electrod using (OA)as plasticizer.

The slope of the calibration curve from Figure (3.4) was 31.57 mv/decade for (WFN-MPA) and 29.62 mv/decade for (WFN-PTA) which were considered adequate from di-valent ion selective electrodes which have a theoretical Nernestain slop of 29.5 mV/decade. The correlation coefficients were (0.9990,0.9998) , the limited of detection was(7×10^{-6} , 6×10^{-6})M and the life times were (35, 40) days for the complexes (WFN-MPA) and (WFN- PTA) respectively , and the linear concentration ranges were (1×10^{-5} - 1×10^{-1}) M for each complex. Response times for warfarin sodium standard solution range (10^{-6} -10^{-1}) M were measured. These parameters are listed in Table (3.2). Electrode parameters were obtained for each electrode which show good responses, stabilities, and gave relative standard deviation values (RSD = 0.552%) for (WFN-MPA) and (RSD = 0.795%) for (WFN-PTA) calculated for average slope values for multiple calibration (n =5). The good stabilities may be due to the high viscosity of the oleic acid (39.2 cST) which attribution to the compatibility of the plasticizer used to the electro-active compound from both structure and composition.

3.3.2. (WFN-MPA ,WFN-PTA+TBP) :

The second membrane was based on Tri-butylphosphate (TBP) as a plasticizer; the calibration curve for these electrodes are shown in Figure (3.5):

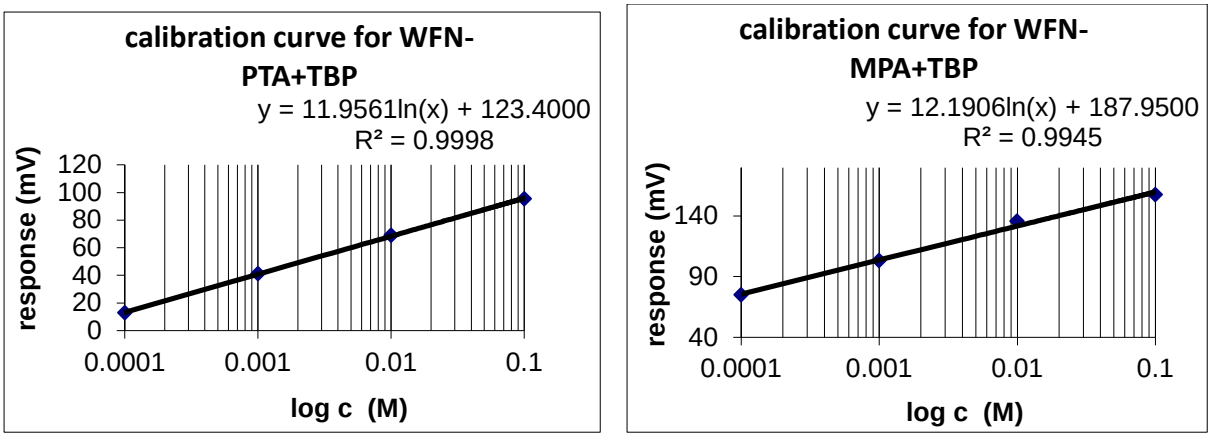


Figure (3.5): Calibration curve of WFN–MPA , WFN-PTA selective electrode using (TBP) as plasticizer.

The potential response of the these electrodes at varying concentration of warfarin sodium was displayed linear range from ($1x10^{-4}$ -$1x10^{-1}$)M for each electrode with slope of 28.07 mV/decade for (WFN-MPA) and 27.53 mV/decade for (WFN-PTA) .The detection limits were (5×10^{-5} ,6×10^{-5})M, the correlation coefficients were (0.9944 ,0.9996), the life times were (25 , 30) days for the complexes (WFN-MPA) and (WFN- PTA) respectively. These parameters are listed in Table (3.2), which gave a relative standard deviation values (RSD = 0.824 %) for (WFN-MPA) and (RSD = 0.955 %) for (WFN-PTA) calculated from average slope values of multiple calibration (n = 5).

3.3.3. (WFN-MPA ,WFN-PTA+ NB) :

Third Membrane was based on Nitrobenzene (NB) as a plasticizer; the calibration curve for these electrodes are shown in Figure (3.6),The calibration curve was calibrated against different concentrations of warfarin sodium gave a slope value of 25.06 mV/decade for (WFN-MPA) and 24.72 mV/decade for (WFN-PTA), linear range for each

electrode were ($1x10^{-5}$ - $1x10^{-1}$) M, detection limits were (5×10^{-6} ,4×10^{-6}) M,the correlation coefficients for the linear range were (0.9994,0.9986),the life times were (14,15) days for the complexes (WFN-MPA) and (WFN- PTA) respectively ,as shown in Table(3.2).

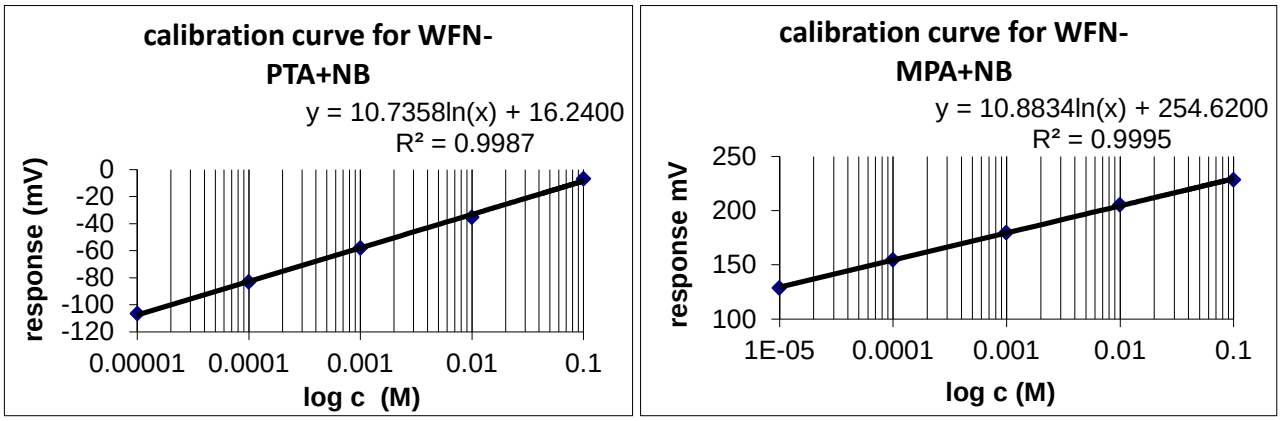


Figure (3.6): Calibration curve of WFN-MPA,WFN-PTA selective electrode using (NB) as plasticizer

The electrode response displayed good stability and reproducibility during measurements, which give relative standard deviation values (RSD = 0.922%) for (WFN-MPA) and (RSD = 0.657%) for (WFN-MPA) where calculated for average slope values for multiple calibration (n =5).

3.3.4. (WFN-MPA ,WFN-PTA+ AP) :

Membrane based on Acetophenone (AP) as a plasticizer are measured at different concentrations of warfarin sodium range from(10^{-6} - 10^{-1}) M. The calibration curves for(WFN-MPA) and (WFN-PTA) gave linear range from ($1x10^{-4}$_$1x10^{-1}$)M as shown in Figure (3-7).

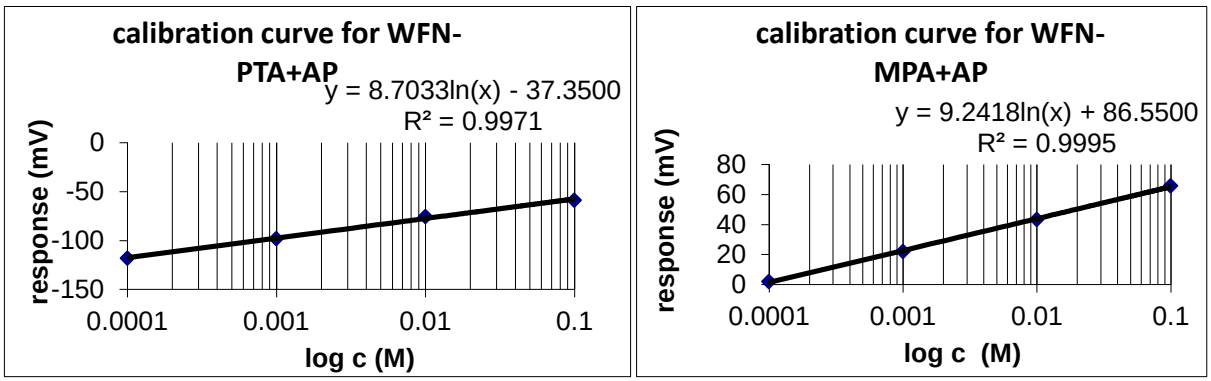


Figure (3.7): Calibration curve of WFN – MPA ,WFN-PTA selective electrode using (AP) as plasticizer.

The linear equations of calibration curves for nernestian part and their slope was(21.28) mV/ decade for (WFN-MPA) and (20.04) mV/ decade for (WFN-PTA). The correlation coefficients for the linear range were (0.9994,0.9970), the life times were (7 , 10) days for the complexes (WFN-MPA) and (WFN- PTA) respectively .These parameters listed in Table (3.2). The life times were short, this may be due to the low viscosity(~1.64 cST) of plasticizer that allowed it to leak out the membrane and electrode was no longer active,Which give relative standard deviation values (RSD = 0.773%) for(WFN-MPA) and (RSD = 0.833%) for(WFN-PTA) where calculated for average slope values for multiple calibration (n = 5).

3.3.5. (WFN-MPA ,WFN-PTA+ DOPH) :

Membrane based on di-octylphthalate(DOPH) as a plasticizer are measured at different concentrations of warfarin sodium range from(10^{-6} - 10^{-1}) M. The calibration curves for each (WFN-MPA) and (WFN-PTA) gave linear range from ($1x10^{-5}$-$1x10^{-1}$) M as shown in Figure. (3.8) .

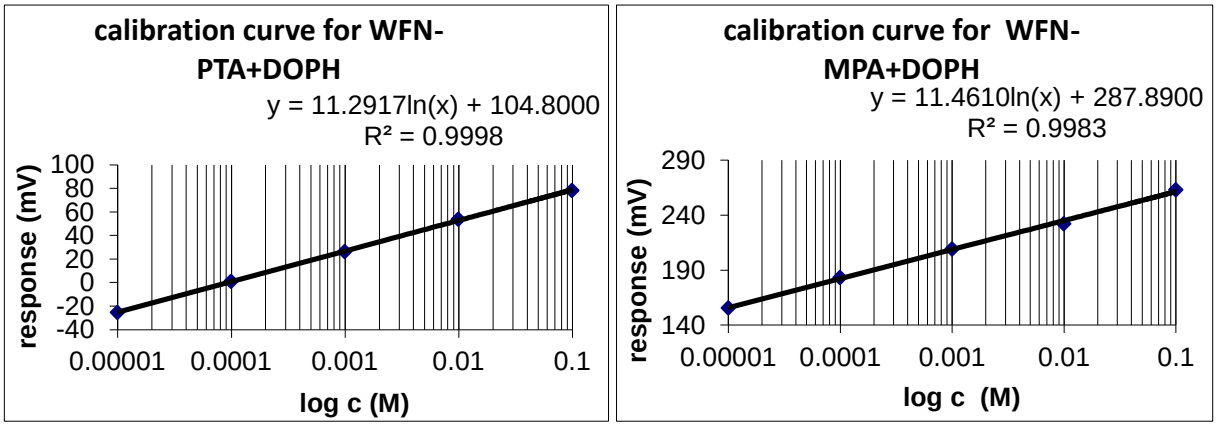


Figure (3.8): Calibration curve of WFN – MPA ,WFN-PTA selective electrode using (DOPH) as plasticizer.

The linear equations of calibration curves for nernestian part and their slope was(26.39) mV/ decade for (WFN-MPA) and (26.00) mV/ decade for (WFN-PTA),the correlation coefficients for the linear range (0.9982,0.9996), the life times were (20 ,25) days for the complexes (WFN-MPA) and (WFN- PTA) respectively . The electrode response displayed good stability and reproducibility during measurements, which give relative standard deviation values (RSD = 0.871%) for (WFN-MPA)

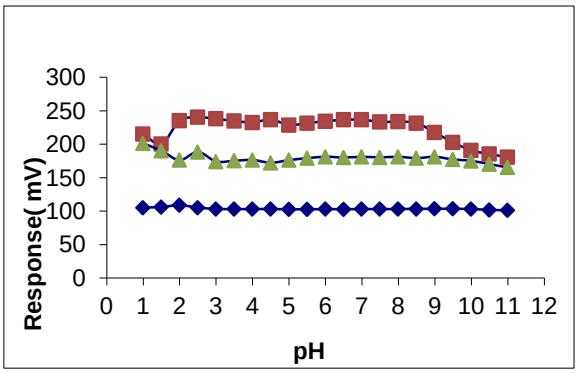
and (RSD = 0.713%) for (WFN-PTA) where calculated for average slope values for multiple calibration (n = 5). This electrode showed good response as shown in Table (3.2). That may be due to the high viscosity ≈ 82 cST, which prevents the leaching of complexes to the external solution and causes a low mobility of ions in the matrix to the membrane.

Table (3.2): The parameters of WFN –MPA,WFN-PTA selective electrodes using different plasticizers.

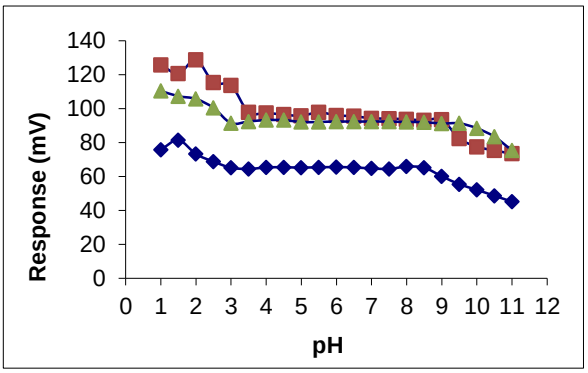
Parameter	Membrane Composition	Plasticizer				
		OA	TBP	NB	AP	DOPH
Slope (mV/dec.)	WFN-MPA	31.57	28.07	25.06	21.28	26.39
	WFN-PTA	29.62	27.53	24.72	20.04	26.00
Detection limit (M)	WFN-MPA	$7x10^{-6}$	$5x10^{-5}$	$5x10^{-6}$	$2\ x10^{-5}$	$6x10^{-6}$
	WFN-PTA	$6x10^{-6}$	$6\ x10^{-5}$	$4\ x10^{-6}$	$4\ x10^{-5}$	$5x10^{-6}$
Correlation coefficient	WFN-MPA	0.9990	0.9944	0.9994	0.9994	0.9982
	WFN-PTA	0.9998	0.9996	0.9986	0.9970	0.9996
Linearity range (M)	WFN-MPA	10^{-5} - 10^{-1}	10^{-4} - 10^{-1}	10^{-5} - 10^{-1}	10^{-4} - 10^{-1}	10^{-5} - 10^{-1}
	WFN-PTA	10^{-5} - 10^{-1}	10^{-4} - 10^{-1}	10^{-5} - 10^{-1}	10^{-4} - 10^{-1}	10^{-5} - 10^{-1}
Life time	WFN-MPA	~35 day	~25 day	~14 day	~7 day	~20 day
	WFN-PTA	~40 day	~30 day	~15 day	~10 day	~25 day

3.4. Effect of pH:

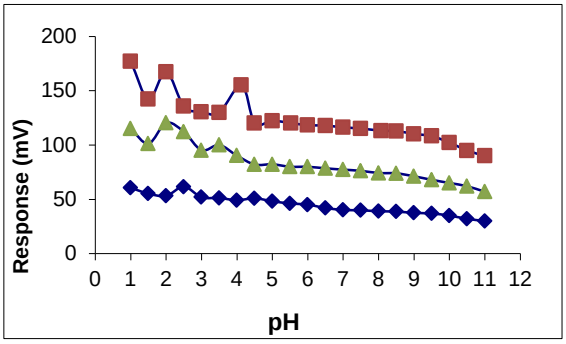
The effect of pH on the electrode potentials for (WFN-MPA), (WFN-PTA) selective membrane electrodes were examined by measuring the e.m.f. of the cell in (WFN)solutions at three different concentrations(10^{-4}, 10^{-3}, 10^{-2} M) for the pH ranged from (1.0-11.0). The pH was adjusted in each time by adding appropriate amounts of hydrochloric acid and/or ammonium hydroxide solution Figure (3.9) .



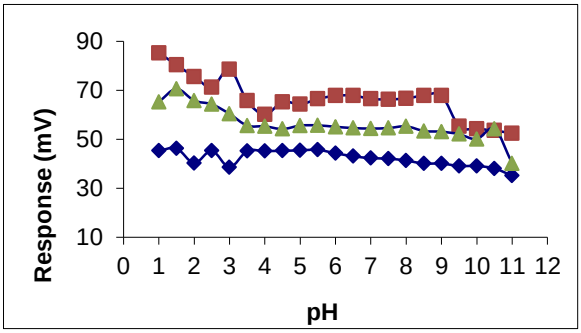
WFN-MPA+OA



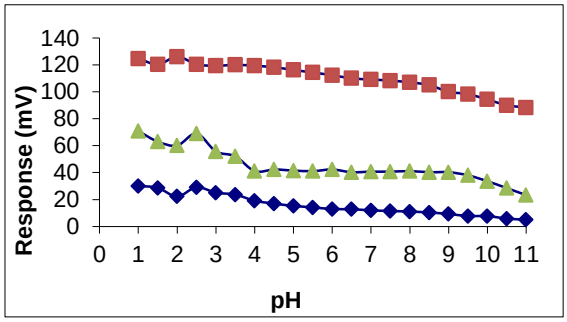
WFN-PTA+OA



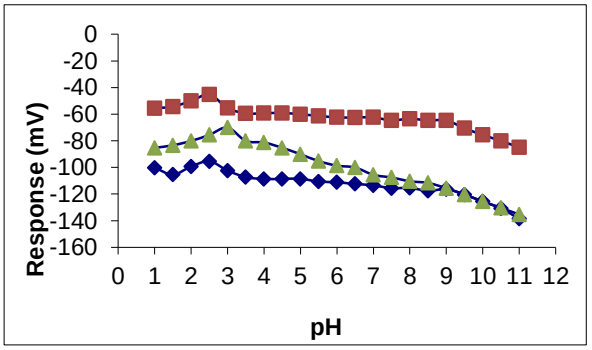
WFN-MPA+TPB



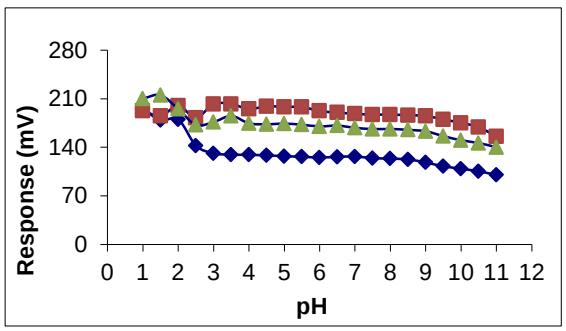
WFN-PTA+TBP



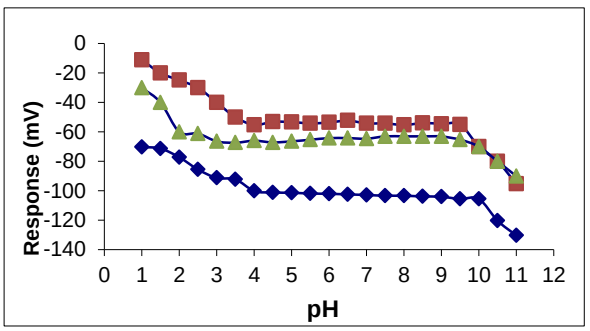
WFN-MPA+NB



WFN-PTA+NB



WFN-MPA+AP



WFN-PTA+AP

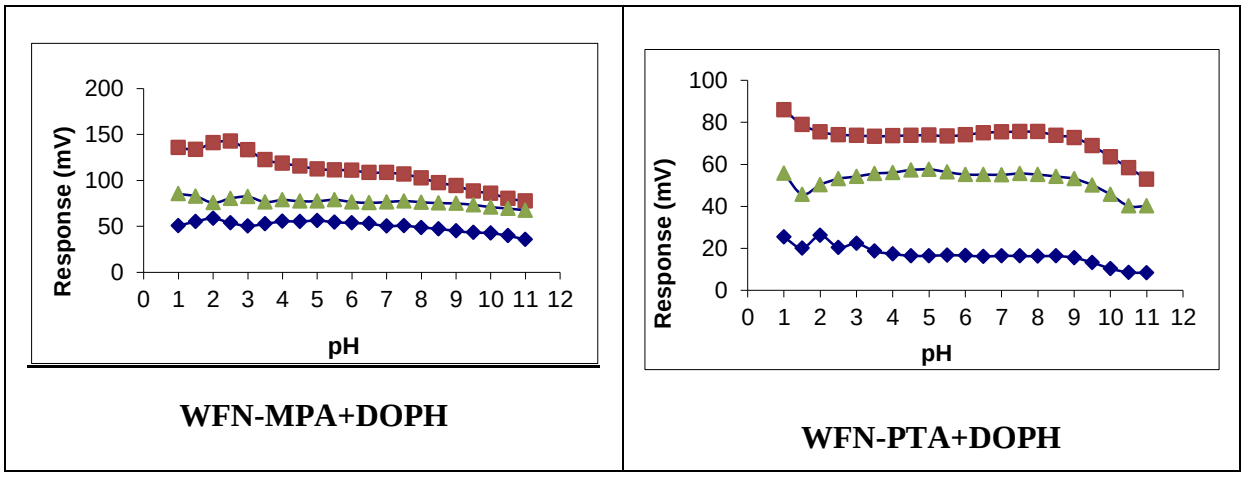


Figure (3.9): Effect of pH on the potential of the warfarin sodium electrodes at concentrations (■10^{-2}, ▲ 10^{-3} and ■ 10^{-4}) M.

The addition of base cause the acidic alpha-hydrogen to ionize. In Figure (3.10) the negative charge can be de localised on the two electronegative oxygen atoms of the carbonyl groups to yield a resonance-stabilised anion. This enhanced stability of the anion allows warfarin to lose a proton and renders the drug acidic with a pKa of 5.0.Warfarin in the free acid form is not very soluble in water and is, therefore, always administered (and is official in the British Pharmacopoeia) as the sodium salt. Upon addition of acide the pair of electrone on the oxygen will be able to accept a proton and thus will form a precipitate in form of keto-enol tautomerism. This means that warfarin exists in two constitutional isomeric forms (tautomers) that are in equilibrium with each other show as Figure (3.11).

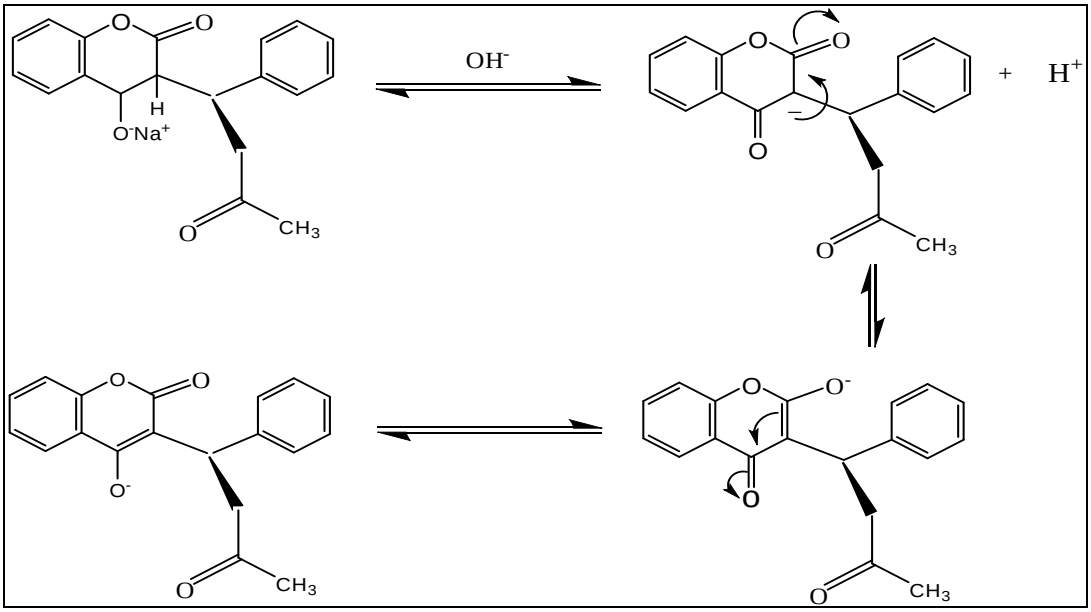


Figure (3.10) : The scheme of degradation products for warfarin sodium in basic media .

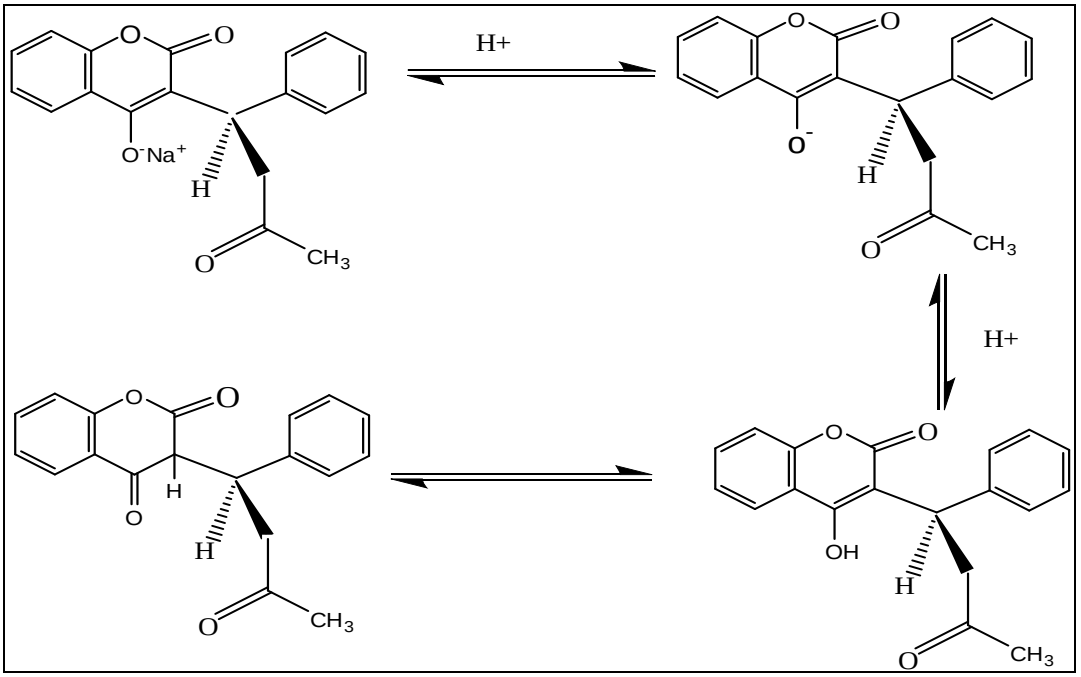


Figure (3.11) : The scheme of degradation products for warfarin sodium in acidic media .

Table (3.3): Working pH ranges for warfarin selective electrodes.

Plasticizer	Membrane Composition	pH range		
		1×10^{-2} M	1×10^{-3} M	1×10^{-4} M
OA	WFN-MPA	4.2 – 8.5	2.5 – 9.5	4.0 – 9.0
	WFN-PTA	3.5 – 9.0	3.8 – 9.5	4.2 – 9.5
TBP	WFN-MPA	5.5 – 9.5	4.5 – 9.8	3.0 – 9.5
	WFN-PTA	5.0 – 9.5	4.0 – 9.8	3.5 – 9.8
NB	WFN-MPA	3.0 – 9.2	4.0 – 9.5	3.2 – 9.6
	WFN-PTA	3.8 – 9.2	4.2 – 8.9	3.5 – 9.6
AP	WFN-MPA	3.0 – 9.0	3.8 – 10.2	3.0 – 10.0
	WFN-PTA	4.5 – 9.8	3.8 – 9.8	4.3 – 10.0
DOPH	WFN-MPA	3.5 – 9.8	4.3 – 9.0	3.0 – 9.5
	WFN-PTA	3.8 – 9.0	4.3 – 9.5	3.5 – 8.5

3.5. Response Time:

The average response time is defined as the time required for the electrode to reach a stable potential within ±1 mV of the final equilibrium value, after the electrode and the reference electrode were immersed in calibration solutions of low and high warfarin sodium concentrations. The response time obviously is dependent on concentration change. The average response time ($t_{95\%}$) of the warfarin sodium membranes (WFN-MPA),(WFN-PTA)were listed in Table (3.4) (3.5) respectively.

Table (3.4): Response time of WFN-MPA electrodes:

Membrane composition	Concentration (M)	Potential (mV) at t/100	Time (s) at 95%	Time (s) at 100%
WFN-MPA + OA	10^{-1}	448.7	12	13
	10^{-2}	420.8	15	19
	10^{-3}	386.2	22	24
	10^{-4}	355.1	27	30
	10^{-5}	323.7	32	33
	10^{-6}	335.4	41	43
WFN-MPA+ TBP	10^{-1}	157.5	16	17
	10^{-2}	135.7	21	23
	10^{-3}	103.1	27	29
	10^{-4}	74.8	30	33
	10^{-5}	77.2	38	40
	10^{-6}	85.6	35	49
WFN-MPA+NB	10^{-1}	228.5	17	18
	10^{-2}	205.6	23	25
	10^{-3}	179.8	31	32
	10^{-4}	154.6	36	39
	10^{-5}	128.7	44	45
	10^{-6}	143.3	49	51
WFN-MPA+ AP	10^{-1}	65.8	19	20
	10^{-2}	43.5	29	31
	10^{-3}	22.1	35	38
	10^{-4}	2.2	42	45

	10^{-5}	12.3	49	52
	10^{-6}	20.4	52	56
WFN-MPA+DOPH	10^{-1}	263.1	13	15
	10^{-2}	232.3	17	20
	10^{-3}	209.3	24	25
	10^{-4}	183.2	32	33
	10^{-5}	155.7	38	40
	10^{-6}	173.1	44	48

Table (3.5): Response time of WFN-PTA electrodes:

Membrane composition	Concentration (M)	Potential (mV) at t/100	Time (s) at 95%	Time (s) at 100%
WFN-PTA + OA	10^{-1}	124.3	10	12
	10^{-2}	95.4	13	16
	10^{-3}	66.1	23	25
	10^{-4}	35.8	29	33
	10^{-5}	6.5	34	38
	10^{-6}	18.5	44	46
WFN-PTA+ TB	10^{-1}	95.4	15	18
	10^{-2}	68.9	22	24
	10^{-3}	41.1	27	30
	10^{-4}	12.9	31	35
	10^{-5}	24.1	40	41
	10^{-6}	35.2	42	50

WFN-PTA+NB	10^{-1}	-6.8	15	17
	10^{-2}	-35.3	18	20
	10^{-3}	-57.9	25	28
	10^{-4}	-83.1	33	35
	10^{-5}	-106.5	41	44
	10^{-6}	-102.1	50	52
WFN-PTA+ AP	10^{-1}	-58.6	20	22
	10^{-2}	-75.4	30	33
	10^{-3}	-97.9	38	40
	10^{-4}	-117.9	44	47
	10^{-5}	-112.7	52	55
	10^{-6}	-95.2	55	59
WFN-PTA+DOPH	10^{-1}	78.3	13	15
	10^{-2}	53.7	17	20
	10^{-3}	26.3	24	25
	10^{-4}	1.1	32	33
	10^{-5}	-25.4	38	40
	10^{-6}	-18.5	44	48

As it is noticed from the Table (3.4),(3.5), the values of response time increase as the concentration decrease. This is attributed to the more time to reach the equilibrium between the complexes in the membrane and the external solution where the concentration of external solution is low**.**

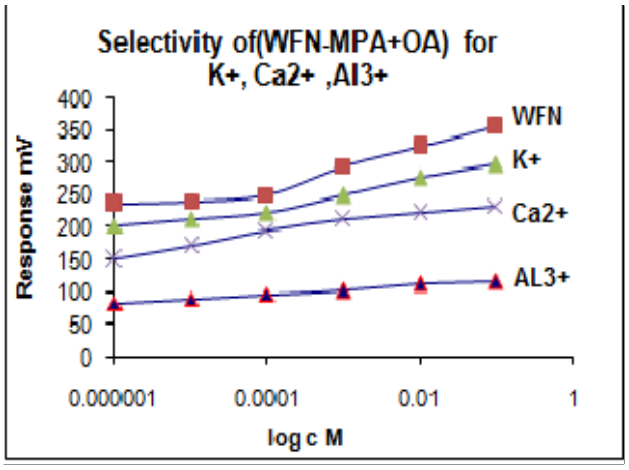
3.6. Selectivity of warfarin sodium Selective electrodes :

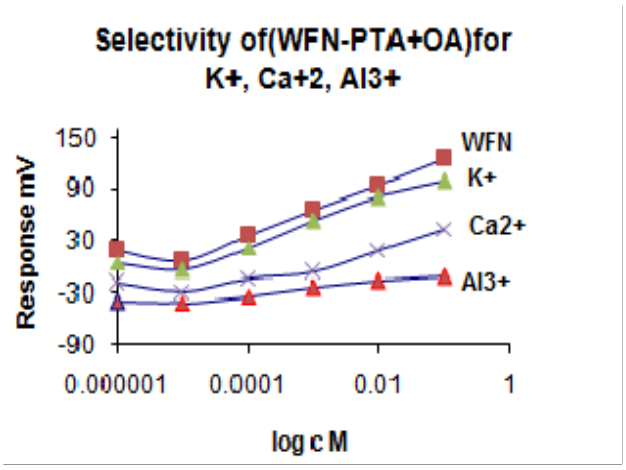
The potentiometric selectivity coefficient of an electrode, as one of the most important characteristics, is defined by its relative response for

the primary ion over the other ions present in the solution. Potentiometric selectivity can be measured with different methods that fall into two main groups, The separate solution method (SSM) , and The matched potential method (MPM). The separate solution method (SSM) is recommended by IUPAC to determine the selectivity coefficient of the ISEs. SSM is based on Nickolsky-Eisenman equation. However, it has been shown that this method suffers some limitations in terms of the values for ions of unequal charges, a non-Nernstain behavior of interfering ions. Therefore another method named the "matched potential method (MPM)" was recommended especially when the primary ion or the interfering ion dissatisfied with the Nernst response or when the involved ions are unequal in charge.

3.6.1. Selectivity measurement by separation method (SSM):

The selectivity of warfarin sodium electrodes was measured by separated solution method for concentrations range (10^{-6} – 10^{-1}) M of warfarin sodium solutions. The concentrations for different ions (K^{+}, Na^{+}, Mg^{2+}, Ca^{2+}, Al^{3+}, $Fe^{3+,}$) and for three amino acids (alanine, proline , serine) was ranged from (10^{-1} to 10^{-6}) M and the potentiometric selective coefficients were calculated by using equation (1-8). The values of $K_{A,B}$ and potential of interference ions are listed in Tables (3.6) to (3.10) for (WFN-MPA) and (3.11) to (3.15) for (WFN-PTA) the selectivities toward the studied species are shown in Figure (3.12) to (3.16):





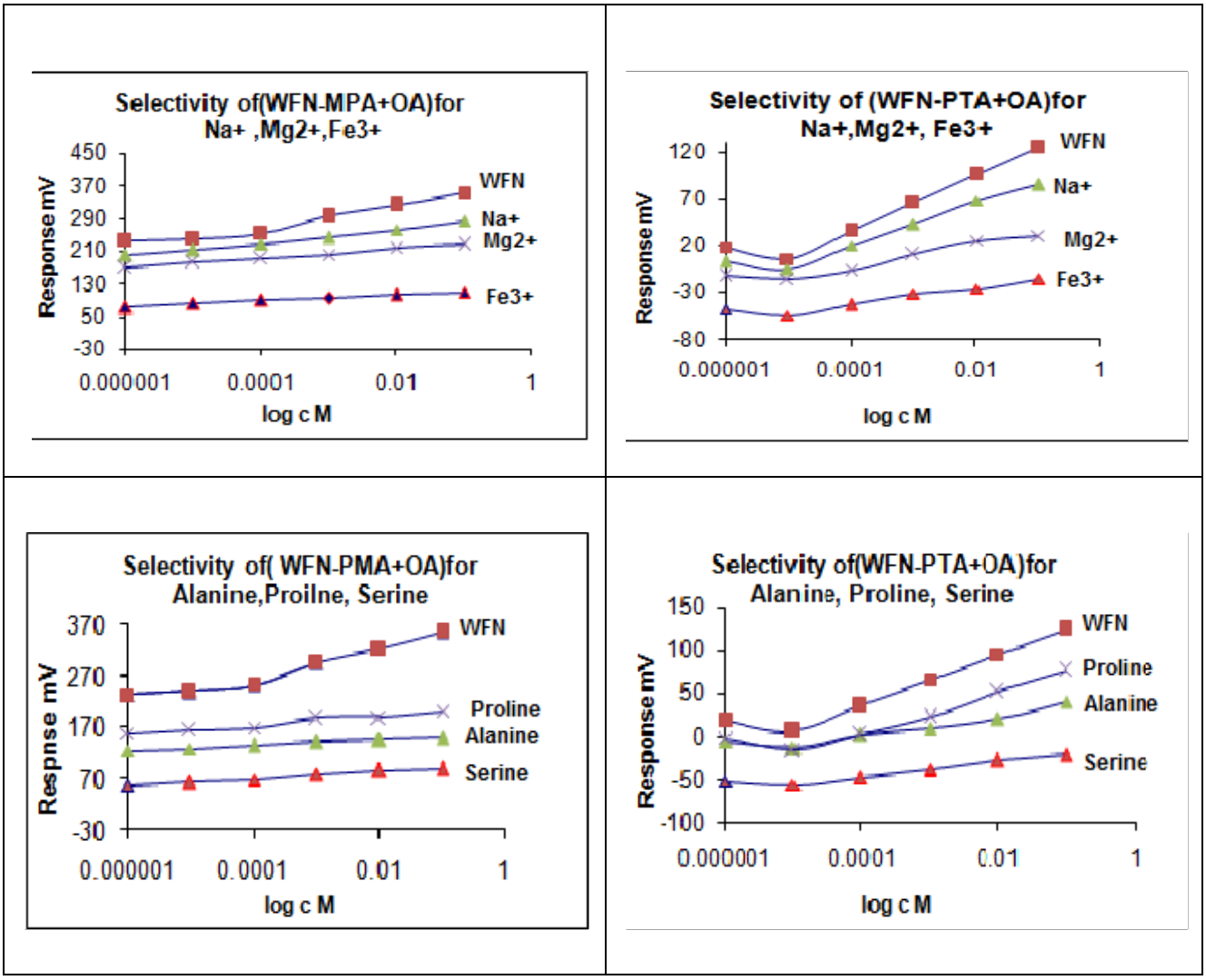
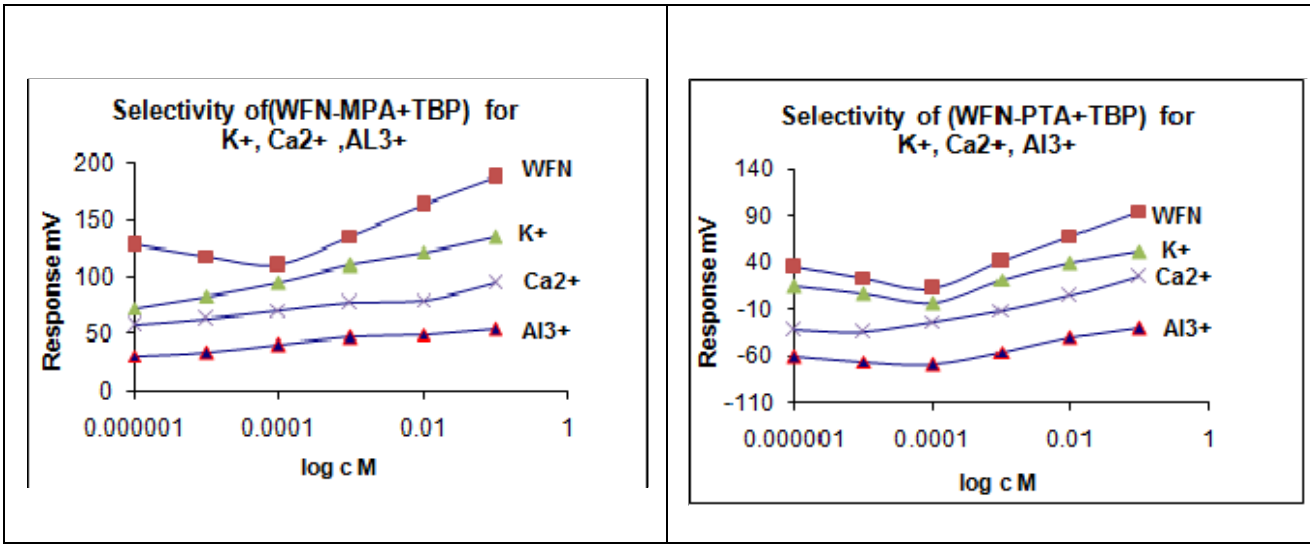


Figure (3. 12): Selectivity of (WFN-MPA+OA) ,(WFN-PTA+OA)and the interfering cations and amino acid by separation solution method.



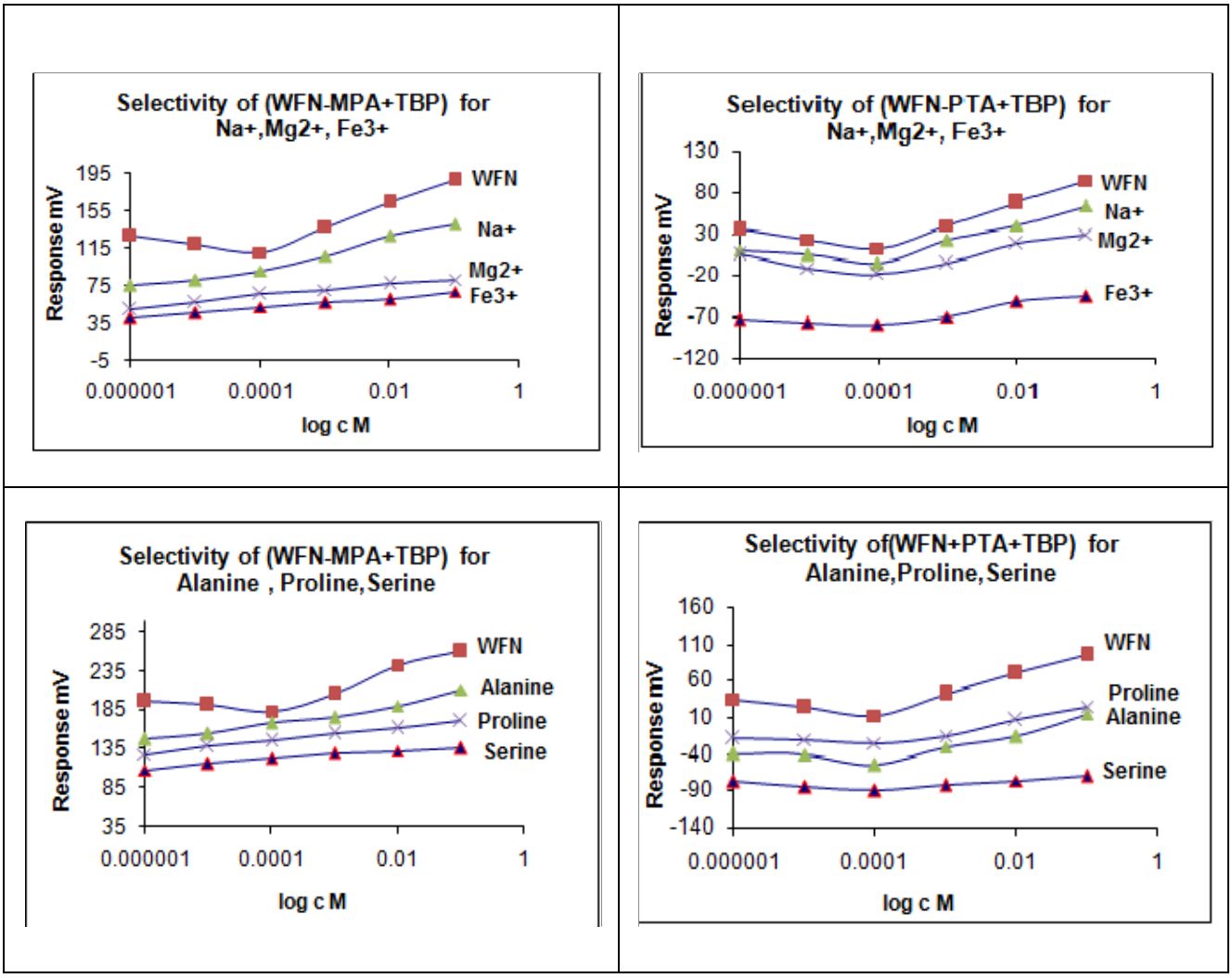
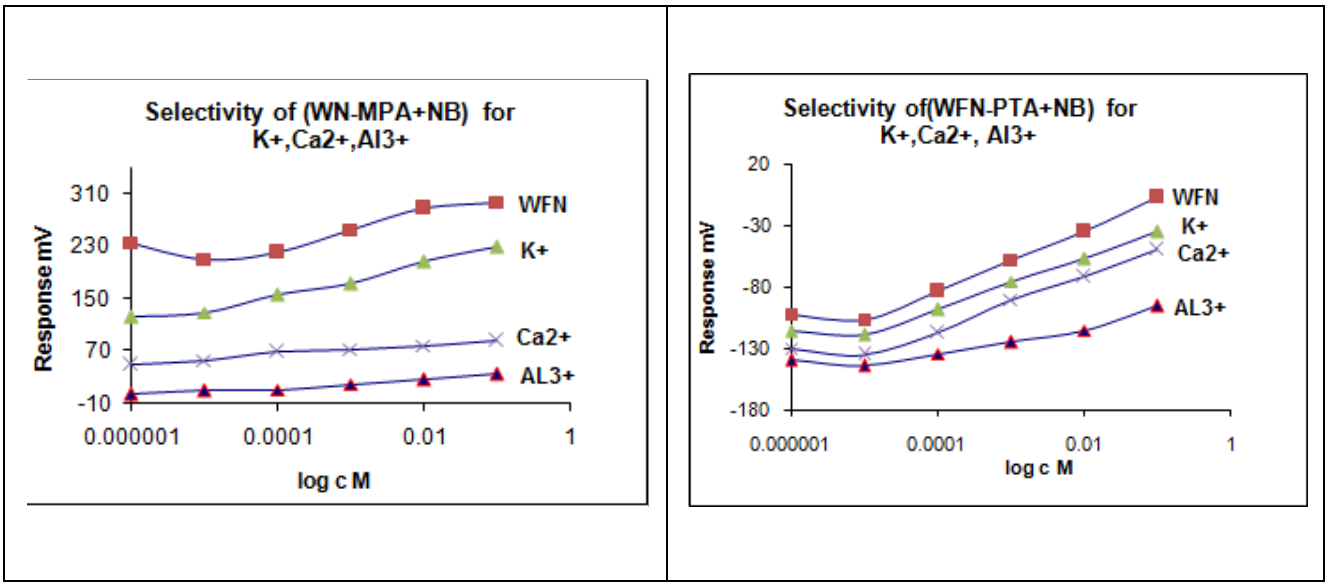


Figure (3. 13): Selectivity of (WFN-MPA+TBP) ,(WFN-PTA+TBP)and the interfering cations and amino acid by separation solution method.



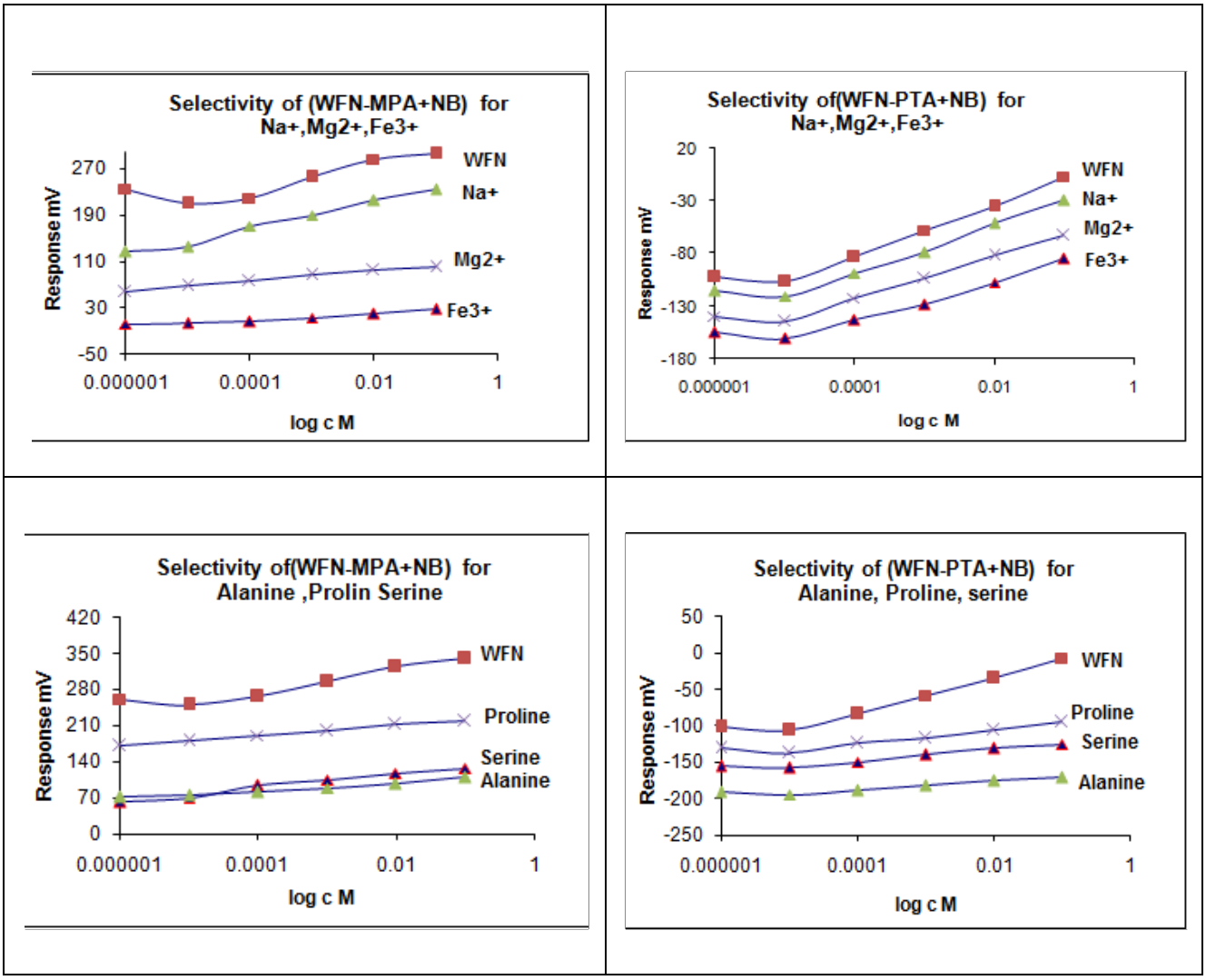
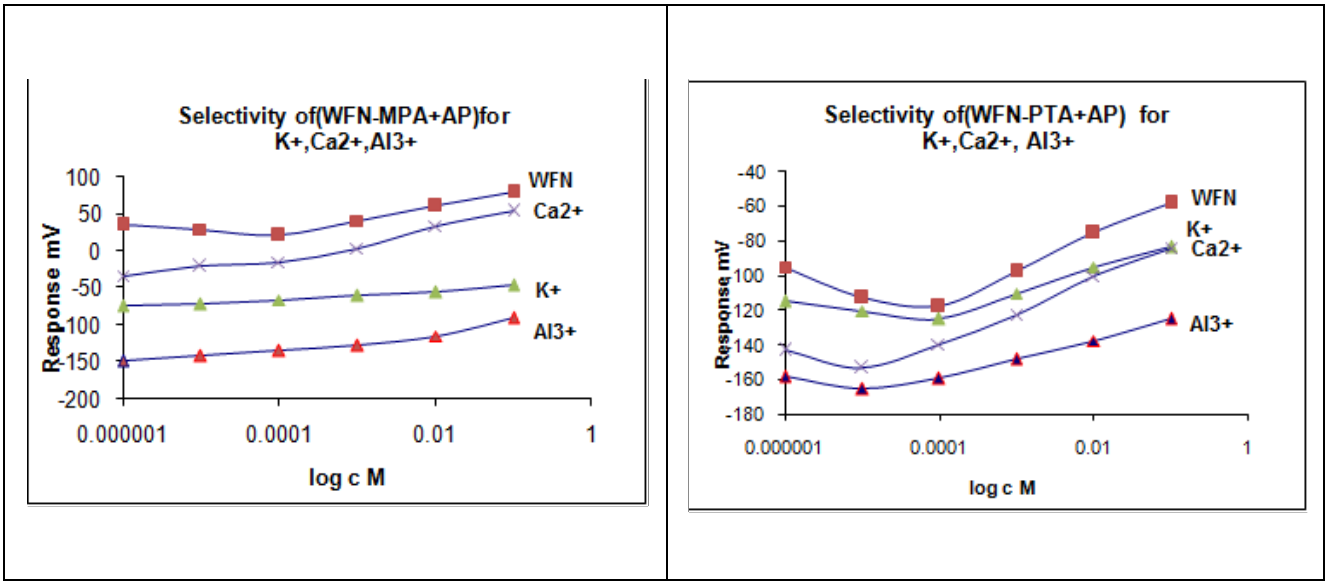


Figure (3. 14): Selectivity of (WFN-MPA+NB) ,(WFN-PTA+NB)and the interfering cations and amino acid by separation solution method.



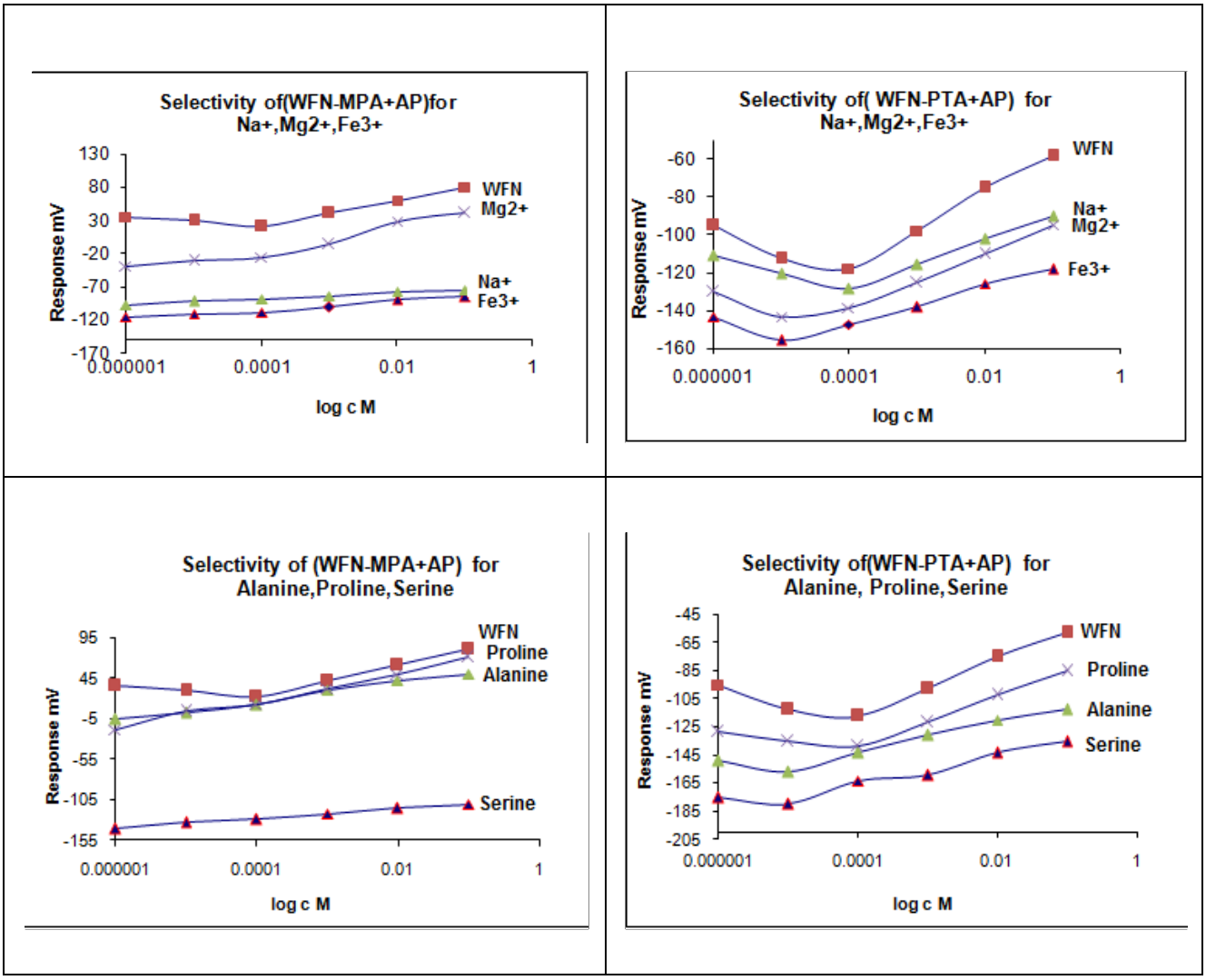
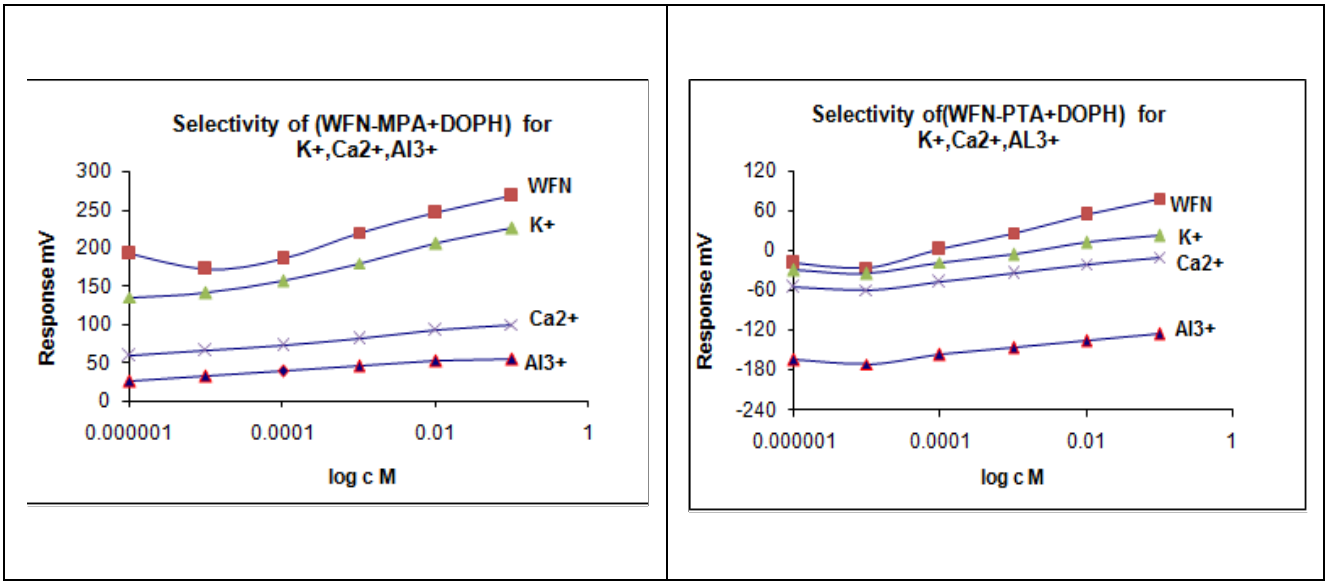


Figure (3. 15): Selectivity of (WFN-MPA+AP) ,(WFN-PTA+AP)and the interfering cations and amino acid by separation solution method.



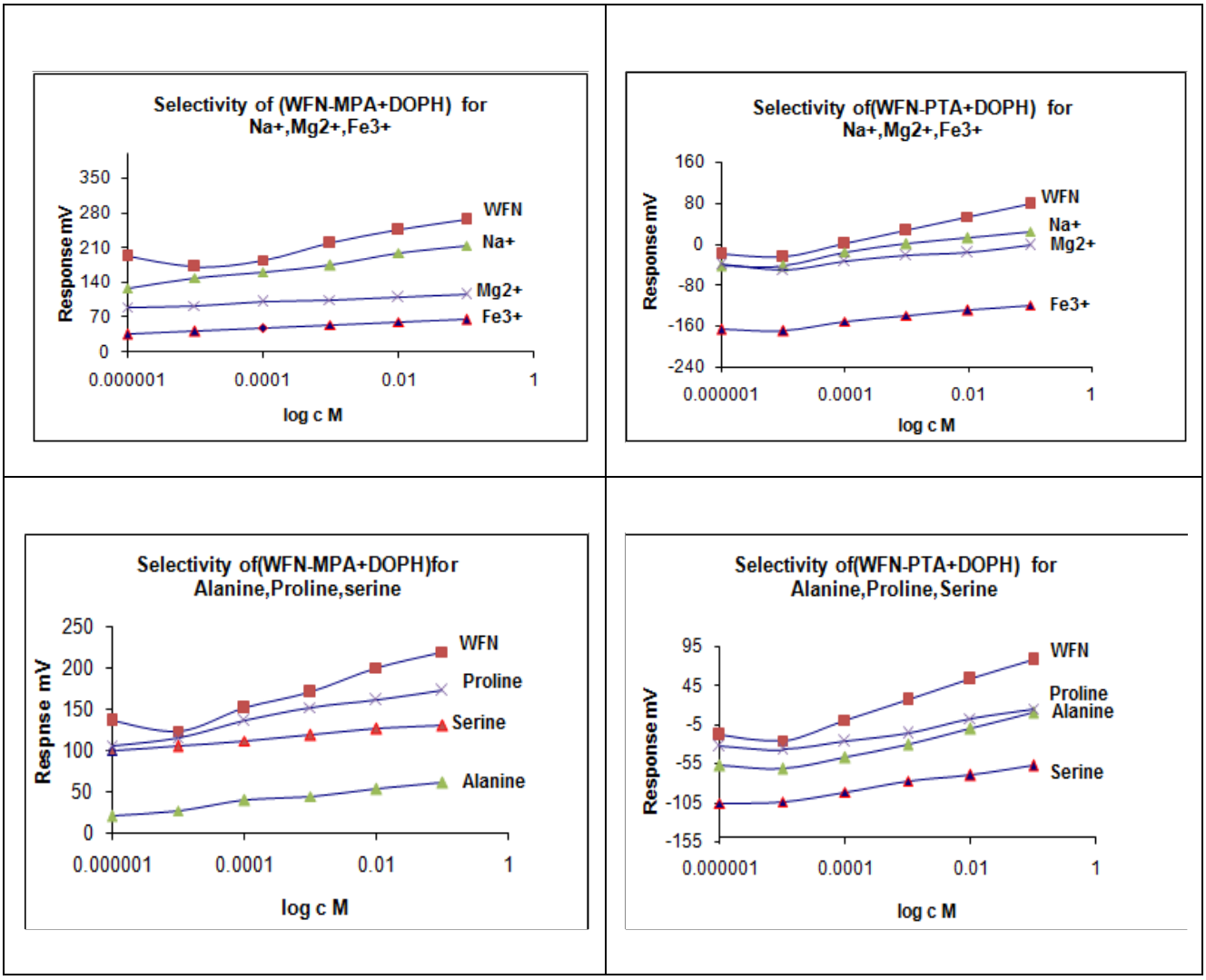


Figure (3.16): Selectivity of (WFN-MPA+DOPH) ,(WFN-PTA+DOPH)and the interfere ing cations and amino acid by separation solution method.

Table (3.6): Selectivity Coefficients for WFN-MPA+OA electrode at different concentrations by separation solution method.

Interfering ions	Concentrations of warfarin sodium (M)											
	10^{-1}		10^{-2}		10^{-3}		10^{-4}		10^{-5}		10^{-6}	
	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$
K^+	295.4	1.023×10^{-2}	275.1	2.551×10^{-2}	249.4	2.997×10^{-2}	222.1	1.113×10^{-1}	211.7	1.131×10^{-1}	202.4	8.382×10^{-2}
Na^+	285.1	4.642×10^{-3}	262.4	9.623×10^{-3}	243.7	1.935×10^{-2}	228.1	1.765×10^{-1}	211.3	1.096×10^{-1}	200.1	7.025×10^{-2}
Ca^{2+}	233.1	2.712×10^{-5}	222.1	4.365×10^{-5}	211.7	5.248×10^{-5}	195.3	1.423×10^{-4}	170.4	1.502×10^{-5}	150.7	1.585×10^{-6}
Mg^{2+}	225.4	1.502×10^{-5}	219.4	3.548×10^{-5}	202.1	2.512×10^{-5}	190.1	9.549×10^{-5}	181.4	3.494×10^{-5}	170.4	7.189×10^{-6}
Al^{3+}	115.7	2.254×10^{-9}	111.2	4.068×10^{-9}	100.7	3.304×10^{-9}	96.4	1.544×10^{-8}	90.1	4.624×10^{-9}	83.4	9.009×10^{-10}
Fe^{3+}	110.7	1.536×10^{-9}	104.7	2.469×10^{-9}	95.4	2.199×10^{-9}	89.3	8.954×10^{-9}	81.7	2.427×10^{-9}	73.4	4.182×10^{-10}
Alanine	150.7	1.537×10^{-7}	147.6	1.434×10^{-6}	142.3	8.066×10^{-6}	136.5	1.561×10^{-4}	130.1	2.154×10^{-4}	125.7	2.326×10^{-4}
Proline	200.1	6.813×10^{-6}	190.1	3.744×10^{-5}	187.3	2.551×10^{-4}	170.3	2.089×10^{-3}	165.3	3.211×10^{-3}	159.7	3.162×10^{-3}
Serine	90.1	1.468×10^{-9}	85.7	1.239×10^{-8}	79.4	6.456×10^{-8}	70.4	9.770×10^{-7}	64.9	1.445×10^{-6}	58.3	1.318×10^{-6}

Table (3.7): Selectivity Coefficients for WFN-MPA+TBP electrode at different concentrations by separation solution method.

Interfering ions	Concentrations of warfarin sodium (M)											
	10^{-1}		10^{-2}		10^{-3}		10^{-4}		10^{-5}		10^{-6}	
	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$
K^+	135.7	9.824×10^{-3}	122.3	2.557×10^{-2}	110.7	1.018×10^{-1}	95.3	2.649×10^{-1}	83.7	4.587×10^{-2}	72.8	7.335×10^{-3}
Na^+	140.3	1.476×10^{-2}	127.4	4.016×10^{-2}	105.8	6.595×10^{-2}	90.7	1.763×10^{-1}	80.3	3.394×10^{-2}	75.4	9.233×10^{-3}
Ca^{2+}	95.4	8.756×10^{-5}	80.3	6.199×10^{-5}	77.3	1.642×10^{-4}	71.4	3.190×10^{-4}	63.4	2.403×10^{-5}	58.5	2.067×10^{-6}
Mg^{2+}	81.3	2.152×10^{-5}	77.4	4.794×10^{-5}	70.8	9.234×10^{-5}	66.1	1.995×10^{-4}	57.3	1.400×10^{-5}	50.2	9.912×10^{-7}
Al^{3+}	55.1	1.679×10^{-6}	50.4	2.034×10^{-6}	47.4	3.668×10^{-6}	40.1	4.285×10^{-6}	33.1	2.401×10^{-7}	30.7	1.754×10^{-8}
Fe^{3+}	68.7	5.602×10^{-6}	60.1	4.802×10^{-6}	57.3	8.814×10^{-6}	52.4	1.274×10^{-5}	45.7	7.328×10^{-7}	40.3	4.106×10^{-8}
Alanine	210.5	1.398×10^{-2}	190.3	1.109×10^{-2}	175.3	7.596×10^{-2}	167.7	2.640×10^{-1}	154.3	4.383×10^{-2}	148.2	1.718×10^{-2}
Proline	170.1	4.346×10^{-4}	161.3	9.177×10^{-4}	153.7	1.187×10^{-2}	145.8	4.022×10^{-2}	138.9	1.167×10^{-2}	127.7	2.950×10^{-3}
Serine	135.8	2.281×10^{-5}	132.7	7.862×10^{-5}	128.7	1.386×10^{-3}	121.8	5.116×10^{-3}	115.9	1.618×10^{-3}	107.2	5.073×10^{-4}

Table (3.8): Selectivity Coefficients for WFN-MPA+NB electrodes at different concentrations by separation solution method.

Interfering ions	Concentrations of warfarin sodium (M)											
	10^{-1}		10^{-2}		10^{-3}		10^{-4}		10^{-5}		10^{-6}	
	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$
K^+	228.1	1.308×10^{-3}	205.6	3.943×10^{-4}	172.8	3.514×10^{-4}	155.3	1.995×10^{-3}	128.7	3.868×10^{-4}	122.8	2.113×10^{-5}
Na^+	235.1	2.560×10^{-3}	215.3	1.001×10^{-3}	190.4	1.901×10^{-3}	171.7	9.623×10^{-3}	135.1	7.148×10^{-4}	126.8	2.901×10^{-5}
Ca^{2+}	85.3	4.642×10^{-10}	78.3	1.957×10^{-10}	72.4	7.286×10^{-10}	68.3	4.731×10^{-9}	55.7	1.111×10^{-9}	48.3	1.555×10^{-11}
Mg^{2+}	101.3	2.154×10^{-9}	95.8	1.049×10^{-9}	87.3	2.844×10^{-9}	75.7	9.624×10^{-9}	68.7	3.868×10^{-9}	57.3	3.687×10^{-11}
Al^{3+}	35.3	2.608×10^{-12}	25.7	5.834×10^{-13}	19.3	1.409×10^{-12}	11.2	4.242×10^{-12}	9.7	1.969×10^{-12}	4.2	2.249×10^{-14}
Fe^{3+}	28.3	1.332×10^{-12}	20.7	3.611×10^{-13}	12.8	7.554×10^{-13}	7.3	7.264×10^{-12}	3.2	1.055×10^{-12}	2.2	1.857×10^{-14}
Alanine	110.7	2.379×10^{-10}	98.3	3.028×10^{-10}	89.4	2.403×10^{-10}	81.3	8.268×10^{-9}	75.4	4.902×10^{-8}	70.7	9.622×10^{-9}
Proline	220.1	8.994×10^{-6}	212.3	1.783×10^{-5}	200.7	1.090×10^{-4}	192.3	7.346×10^{-4}	181.3	1.322×10^{-3}	170.1	1.387×10^{-4}
Serine	128.1	1.272×10^{-9}	118.3	2.079×10^{-9}	105.4	1.122×10^{-8}	93.7	5.503×10^{-8}	70.1	2.942×10^{-8}	62.3	4.284×10^{-9}

Table (3.9): Selectivity Coefficients for WFN-MPA+AP electrode at different concentrations by separation solution method.

Interfering ions	Concentrations of warfarin sodium (M)											
	10^{-1}		10^{-2}		10^{-3}		10^{-4}		10^{-5}		10^{-6}	
	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$
K^+	-45.7	4.114×10^{-7}	-55.3	1.339×10^{-6}	-60.4	6.960×10^{-6}	-66.4	3.659×10^{-5}	-71.6	7.466×10^{-6}	-75.1	2.375×10^{-6}
Na^+	-75.3	1.324×10^{-8}	-77.3	1.024×10^{-7}	-83.4	4.733×10^{-7}	-88.4	2.797×10^{-6}	-91.3	7.466×10^{-7}	-97.5	1.732×10^{-7}
Ca^{2+}	54.1	1.514×10^{-2}	33.7	4.412×10^{-3}	3.7	3.949×10^{-4}	-14.8	1.403×10^{-3}	-20.7	9.054×10^{-6}	-33.7	3.001×10^{-7}
Mg^{2+}	40.3	3.018×10^{-3}	28.4	7.509×10^{-4}	-5.7	3.824×10^{-3}	-25.7	4.260×10^{-3}	-30.2	9.432×10^{-4}	-38.7	1.672×10^{-4}
Al^{3+}	-90.1	4.936×10^{-10}	-115.2	5.653×10^{-11}	-128.3	2.483×10^{-11}	-135.7	2.386×10^{-11}	-142.4	9.215×10^{-13}	-149.3	4.047×10^{-14}
Fe^{3+}	-85.1	8.855×10^{-10}	-90.0	1.075×10^{-9}	-101.0	6.036×10^{-10}	-108.4	2.173×10^{-10}	-110.5	3.659×10^{-11}	-115.3	2.153×10^{-12}
Alanine	50.2	3.036×10^{-2}	42.1	1.178×10^{-1}	30.5	2.863×10^{-1}	12.4	3.659×10^{-1}	2.1	4.113×10^{-2}	-5.3	8.294×10^{-3}
Proline	70.2	3.144×10^{-1}	50.1	3.010×10^{-1}	32.4	3.575×10^{-1}	12.7	3.790×10^{-1}	4.2	5.258×10^{-2}	-18.9	1.692×10^{-3}
Serine	-110.7	2.064×10^{-10}	-115.7	1.150×10^{-9}	-122.3	5.018×10^{-9}	-129.4	2.319×10^{-8}	-133.7	5.258×10^{-9}	-140.8	1.098×10^{-9}

Table (3.10): Selectivity Coefficients for WFN-MPA+DOPH electrode at different concentrations by separation solution method.

Interfering ions	Concentrations of warfarin sodium (M)											
	10^{-1}		10^{-2}		10^{-3}		10^{-4}		10^{-5}		10^{-6}	
	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$
K^+	225.3	1.995×10^{-2}	205.3	2.208×10^{-2}	180.1	2.489×10^{-2}	157.3	7.586×10^{-2}	141.2	5.598×10^{-2}	135.7	5.346×10^{-3}
Na^+	215.2	7.870×10^{-3}	200.1	1.368×10^{-2}	175.4	1.614×10^{-2}	162.3	1.202×10^{-1}	150.4	1.306×10^{-1}	129.2	2.938×10^{-3}
Ca^{2+}	100.4	6.368×10^{-8}	92.2	6.607×10^{-8}	81.7	9.120×10^{-8}	72.3	3.019×10^{-7}	65.7	1.690×10^{-7}	59.4	4.742×10^{-9}
Mg^{2+}	115.3	2.512×10^{-7}	110.8	3.664×10^{-7}	105.7	8.318×10^{-7}	100.7	4.130×10^{-6}	94.2	2.333×10^{-6}	90.7	8.472×10^{-8}
Al^{3+}	55.3	6.808×10^{-10}	51.7	1.399×10^{-10}	46.2	1.094×10^{-9}	39.7	3.221×10^{-9}	32.4	1.151×10^{-9}	25.7	2.118×10^{-11}
Fe^{3+}	65.3	1.710×10^{-9}	61.8	1.862×10^{-9}	55.4	2.553×10^{-9}	49.3	7.798×10^{-9}	41.3	2.612×10^{-9}	35.7	5.321×10^{-11}
Alanine	60.2	2.349×10^{-7}	52.7	7.217×10^{-7}	43.9	5.412×10^{-6}	38.7	2.154×10^{-5}	26.7	9.905×10^{-5}	20.1	1.525×10^{-5}
Proline	172.3	1.101×10^{-2}	160.3	2.196×10^{-2}	152.3	1.778×10^{-1}	135.1	2.239×10^{-1}	115.4	4.917×10^{-1}	105.7	5.623×10^{-2}
Serine	130.1	1.920×10^{-4}	125.7	7.943×10^{-4}	118.6	7.012×10^{-3}	111.4	2.304×10^{-2}	104.7	1.761×10^{-1}	100.1	3.286×10^{-2}

Table (3.11): Selectivity Coefficients for WFN-PTA+OA electrode at different concentrations by separation solution method.

Interfering ions	Concentrations of warfarin sodium (M)											
	10^{-1}		10^{-2}		10^{-3}		10^{-4}		10^{-5}		10^{-6}	
	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$
K^+	100.1	1.522×10^{-1}	82.3	3.609×10^{-1}	54.1	3.932×10^{-1}	22.8	3.638×10^{-1}	-3.4	4.813×10^{-1}	5.3	3.581×10^{-1}
Na^+	85.1	4.739×10^{-2}	68.2	1.205×10^{-1}	42.7	1.619×10^{-1}	20.1	2.948×10^{-1}	-5.1	4.217×10^{-1}	3.4	1.758×10^{-1}
Ca^{2+}	45.3	6.778×10^{-4}	20.4	2.926×10^{-4}	-5.7	1.187×10^{-4}	-12.3	2.371×10^{-4}	-27.6	2.317×10^{-4}	-18.7	5.537×10^{-5}
Mg^{2+}	30.7	2.178×10^{-4}	25.6	4.384×10^{-4}	10.7	4.249×10^{-4}	-7.6	3.418×10^{-4}	-15.3	6.031×10^{-4}	-12.7	8.829×10^{-5}
Al^{3+}	-10.7	5.918×10^{-6}	-15.7	8.177×10^{-6}	-24.3	8.809×10^{-6}	-32.4	1.066×10^{-5}	-40.1	1.281×10^{-5}	-39.7	1.076×10^{-6}
Fe^{3+}	-15.2	4.138×10^{-6}	-25.7	3.786×10^{-6}	-31.4	5.071×10^{-6}	-42.6	4.823×10^{-6}	-54.3	4.245×10^{-6}	-47.3	5.957×10^{-7}
Alanine	39.7	1.386×10^{-3}	20.1	2.858×10^{-3}	10.3	1.303×10^{-2}	2.4	7.441×10^{-2}	-12.4	2.390×10^{-1}	-5.7	1.522×10^{-1}
Proline	77.3	2.583×10^{-2}	52.1	3.445×10^{-2}	22.4	3.339×10^{-2}	2.2	7.326×10^{-2}	-15.2	1.922×10^{-1}	-1.4	2.127×10^{-1}
Serine	-20.4	1.293×10^{-5}	-27.6	6.992×10^{-5}	-37.6	3.138×10^{-4}	-46.7	1.632×10^{-3}	-55.4	8.427×10^{-3}	-51.2	4.428×10^{-3}

Table (3.12): Selectivity Coefficients for WFN-PTA+TBP electrode at different concentrations by separation solution method.

Interfering ions	Concentrations of warfarin sodium (M)											
	10^{-1}		10^{-2}		10^{-3}		10^{-4}		10^{-5}		10^{-6}	
	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$
K^+	51.4	2.512×10^{-2}	40.1	8.969×10^{-2}	22.4	2.089×10^{-1}	-2.7	2.708×10^{-1}	7.5	2.491×10^{-1}	15.4	1.905×10^{-1}
Na^+	65.4	8.111×10^{-2}	41.2	9.834×10^{-2}	22.1	2.037×10^{-1}	-5.4	2.160×10^{-1}	5.7	2.142×10^{-1}	10.7	1.286×10^{-1}
Ca^{2+}	25.4	9.006×10^{-4}	4.3	4.476×10^{-4}	-10.7	4.134×10^{-4}	-22.4	5.204×10^{-4}	-34.2	7.586×10^{-5}	-31.4	7.586×10^{-6}
Mg^{2+}	30.2	1.346×10^{-3}	18.2	1.433×10^{-3}	-5.4	6.433×10^{-4}	-19.3	6.747×10^{-4}	-10.7	1.716×10^{-4}	5.4	8.248×10^{-5}
Al^{3+}	-30.1	5.879×10^{-6}	-40.6	4.833×10^{-6}	-55.2	3.142×10^{-6}	-67.9	2.476×10^{-6}	-65.4	2.573×10^{-7}	-59.9	3.466×10^{-8}
Fe^{3+}	-45.3	1.647×10^{-6}	-51.4	1.956×10^{-6}	-69.7	9.330×10^{-7}	-80.1	8.916×10^{-7}	-77.5	9.342×10^{-8}	-73.4	1.119×10^{-8}
Alanine	15.4	1.233×10^{-3}	-15.7	8.388×10^{-4}	-30.1	2.576×10^{-3}	-55.2	3.339×10^{-3}	-40.1	4.629×10^{-3}	-39.7	1.886×10^{-3}
Proline	25.4	2.848×10^{-3}	7.2	5.706×10^{-3}	-15.2	8.969×10^{-3}	-25.4	4.117×10^{-2}	-20.1	2.470×10^{-2}	-18.3	1.134×10^{-2}
Serine	-70.1	9.589×10^{-7}	-76.2	5.292×10^{-6}	-81.7	3.424×10^{-5}	-89.3	1.921×10^{-4}	-85.4	1.043×10^{-4}	-77.3	8.113×10^{-5}

Table (3.13): Selectivity Coefficients for WFN-PTA+NB electrodes at different concentrations by separation solution method.

Interfering ions	Concentrations of warfarin sodium (M)											
	10^{-1}		10^{-2}		10^{-3}		10^{-4}		10^{-5}		10^{-6}	
	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$
K^+	-35.4	6.952×10^{-2}	-57.3	1.286×10^{-1}	-75.3	1.975×10^{-1}	-98.5	2.379×10^{-1}	-118.9	3.148×10^{-1}	-115.7	2.814×10^{-1}
Na^+	-29.1	1.251×10^{-1}	-51.4	2.229×10^{-1}	-79.1	1.386×10^{-1}	-99.0	2.271×10^{-1}	-120.7	2.661×10^{-1}	-115.7	2.814×10^{-1}
Ca^{2+}	-50.1	5.584×10^{-3}	-71.4	3.455×10^{-3}	-90.4	1.528×10^{-3}	-117.2	4.163×10^{-4}	-135.1	2.198×10^{-4}	-130.1	7.352×10^{-5}
Mg^{2+}	-62.7	1.725×10^{-3}	-81.7	1.323×10^{-3}	-104.3	4.183×10^{-4}	-122.4	2.564×10^{-4}	-145.2	8.574×10^{-5}	-139.7	3.004×10^{-5}
Al^{3+}	-95.4	5.571×10^{-5}	-115.4	2.649×10^{-5}	-124.3	2.045×10^{-5}	-134.2	1.833×10^{-5}	-143.7	1.402×10^{-5}	-139.2	3.133×10^{-6}
Fe^{3+}	-84.7	1.476×10^{-4}	-107.6	5.481×10^{-5}	-128.7	1.357×10^{-5}	-143.2	7.921×10^{-6}	-161.1	2.848×10^{-6}	-155.3	6.985×10^{-7}
Alanine	-170.4	2.379×10^{-7}	-175.3	2.148×10^{-6}	-181.4	1.001×10^{-5}	-189.3	5.017×10^{-5}	-194.7	2.686×10^{-4}	-190.4	2.661×10^{-4}
Proline	-94.7	2.762×10^{-4}	-105.7	1.412×10^{-3}	-117.8	3.757×10^{-3}	-123.7	2.271×10^{-2}	-137.8	5.405×10^{-2}	-130.1	7.352×10^{-2}
Serine	-125.1	1.624×10^{-5}	-130.4	1.412×10^{-4}	-139.4	5.017×10^{-4}	-149.7	2.012×10^{-3}	-157.6	8.534×10^{-3}	-155.4	6.952×10^{-3}

Table (3.14): Selectivity Coefficients for WFN-PTA+AP electrode at different concentrations by separation solution method.

Interfering ions	Concentrations of warfarin sodium (M)											
	10^{-1}		10^{-2}		10^{-3}		10^{-4}		10^{-5}		10^{-6}	
	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$
K^+	-83.4	5.754×10^{-2}	-95.2	1.023×10^{-1}	-110.4	2.371×10^{-1}	-125.4	4.217×10^{-1}	-120.4	4.121×10^{-1}	-115.2	1.011×10^{-1}
Na^+	-90.4	2.570×10^{-2}	-102.4	4.467×10^{-2}	-115.7	1.288×10^{-1}	-128.7	2.884×10^{-1}	-120.4	4.121×10^{-1}	-111.2	1.585×10^{-1}
Ca^{2+}	-84.1	1.679×10^{-2}	-100.4	5.623×10^{-3}	-122.4	1.884×10^{-3}	-139.7	8.128×10^{-4}	-153.2	9.440×10^{-3}	-143.5	3.846×10^{-6}
Mg^{2+}	-94.7	4.955×10^{-3}	-110.4	1.778×10^{-3}	-125.1	1.380×10^{-3}	-138.4	9.441×10^{-4}	-143.2	9.441×10^{-5}	-130.4	1.738×10^{-5}
Al^{3+}	-125.4	9.840×10^{-5}	-137.6	3.597×10^{-5}	-148.3	3.013×10^{-5}	-159.3	1.828×10^{-5}	-165.7	1.035×10^{-6}	-158.7	6.653×10^{-8}
Fe^{3+}	-118.3	2.228×10^{-4}	-125.7	1.416×10^{-4}	-138.2	9.638×10^{-5}	-147.3	7.278×10^{-5}	-155.7	3.273×10^{-6}	-143.4	3.873×10^{-7}
Alanine	-112.7	1.972×10^{-3}	-120.4	5.623×10^{-3}	-131.4	2.113×10^{-2}	-143.8	5.069×10^{-2}	-157.6	5.689×10^{-3}	-149.7	1.884×10^{-3}
Proline	-85.7	4.416×10^{-2}	-102.7	4.315×10^{-2}	-122.4	5.957×10^{-2}	-139.5	8.318×10^{-2}	-135.7	7.079×10^{-2}	-128.7	2.113×10^{-2}
Serine	-135.7	1.396×10^{-4}	-143.7	3.846×10^{-4}	-159.7	8.128×10^{-4}	-163.7	5.129×10^{-3}	-180.4	4.121×10^{-4}	-175.3	9.886×10^{-5}

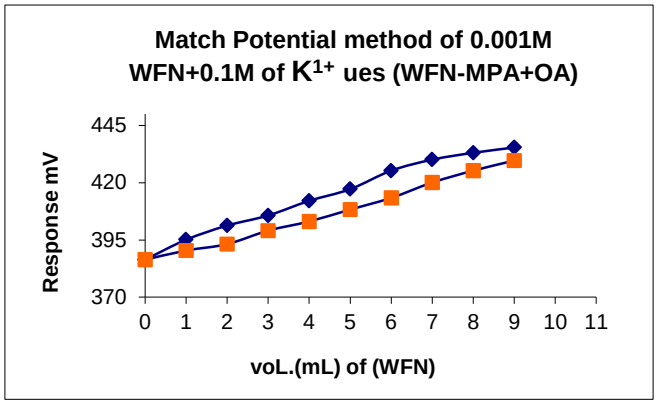
Table (3.15): Selectivity Coefficients for WFN-PTA+DOPH electrode at different concentrations by separation solution method.

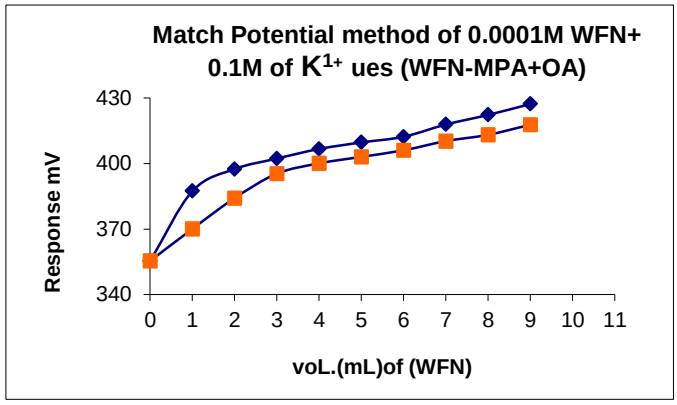
Interfering ions	Concentrations of warfarin sodium (M)											
	10^{-1}		10^{-2}		10^{-3}		10^{-4}		10^{-5}		10^{-6}	
	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$
K^+	22.4	7.079×10^{-3}	11.4	2.361×10^{-2}	-5.7	5.878×10^{-2}	-18.3	1.794×10^{-1}	-35.7	4.016×10^{-1}	-30.1	3.579×10^{-1}
Na^+	25.1	8.992×10^{-3}	12.4	2.579×10^{-2}	1.4	1.102×10^{-1}	-15.4	2.319×10^{-1}	-42.4	2.219×10^{-1}	-41.5	1.304×10^{-1}
Ca^{2+}	-10.4	1.226×10^{-4}	-20.4	1.413×10^{-4}	-34.6	1.438×10^{-4}	-48.6	1.226×10^{-2}	-59.7	4.795×10^{-2}	-55.3	3.843×10^{-2}
Mg^{2+}	-1.5	2.696×10^{-4}	-15.7	2.142×10^{-4}	-21.5	4.587×10^{-4}	-34.2	4.388×10^{-4}	-49.7	3.676×10^{-4}	-40.1	1.476×10^{-4}
Al^{3+}	-125.3	3.179×10^{-9}	-135.7	2.406×10^{-9}	-146.7	2.214×10^{-9}	-157.9	1.647×10^{-9}	-171.4	1.121×10^{-9}	-165.3	2.248×10^{-10}
Fe^{3+}	-118.3	5.908×10^{-9}	-129.4	4.204×10^{-9}	-138.6	4.536×10^{-9}	-150.4	3.199×10^{-9}	-169.4	1.338×10^{-9}	-165.7	2.170×10^{-10}
Alanine	10.3	2.424×10^{-3}	-10.4	3.425×10^{-3}	-30.5	6.537×10^{-3}	-47.6	1.339×10^{-2}	-61.4	4.125×10^{-2}	-57.3	3.219×10^{-2}
Proline	15.7	3.911×10^{-3}	3.4	1.162×10^{-2}	-15.7	2.424×10^{-2}	-26.8	8.451×10^{-2}	-37.4	3.455×10^{-1}	-32.4	2.920×10^{-1}
Serine	-56.7	6.422×10^{-6}	-69.5	1.826×10^{-5}	-76.8	1.083×10^{-4}	-91.4	2.769×10^{-4}	-103.2	1.018×10^{-3}	-105.7	4.427×10^{-4}

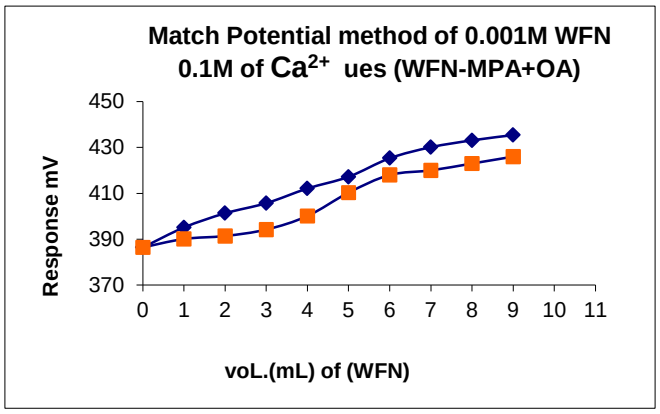
In general, when the value of selectivity coefficient, which represent the potential difference between the interfering ion and the analyte, is less than one, the electrode is respond to analyte more than interfering ion, while when it is higher than one,the electrode starts its response to the interfering ion mor than analyte .The results in Tables (3.6) to (3.15) showed that the selectivity coefficients for monovalent interfering ions is in the order mono> di> trivalent.This may be attributed to the difference in ionic size, mobility and permeability. When the concentration of monovalent ion decreases, the difference in potential measurement decrease. Therefore, the selectivity coefficient increases and the interference of monovalent ion is also increased. An inorganic cations does not interfere because of difference in ionic size, mobility and permeability.

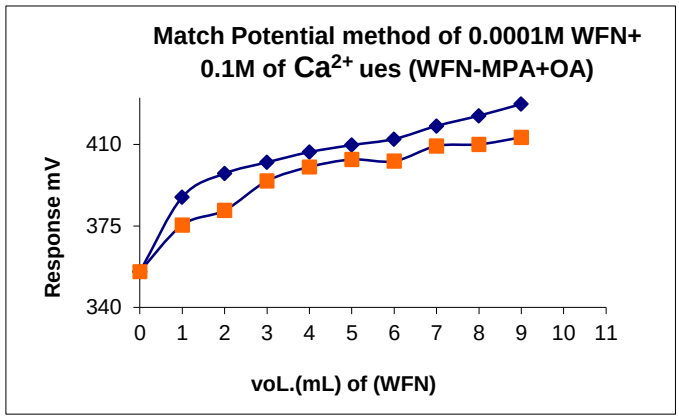
3.6.2. Selectivity measurement by Match potential method (MPM):

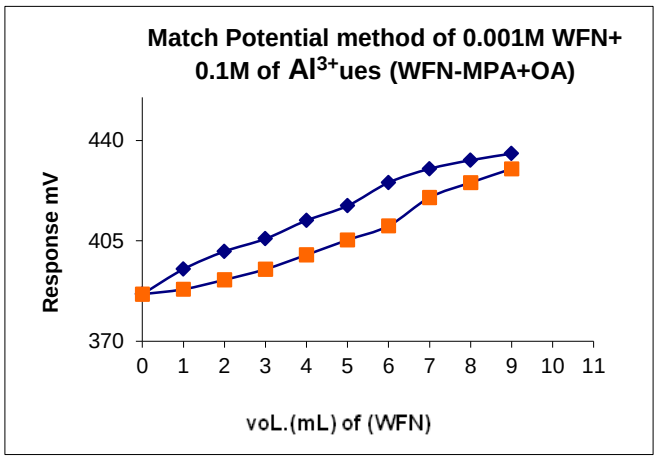
In this method the selectivity coefficient is given by using equation (1- 6) is defined by the ratio of the activity of the primary ion relative to an interfering ion when they generate identical potentials in the same reference solution. In this method both monovalent ions are treated in the same manner, and the valence of the ions does not influence the selectivity coefficient. The results of selectivity coefficient are shown in Figures. (3.17) to (3.21) for (WFN-MPA), (3.22) to (3.26) for (WFN-PTA) and in the Table (3.16) and (3.17) were calculated from the concentration of the interfering ion which endued the same amount of the potential change as that induced by the increase of the concentration of primary ion.

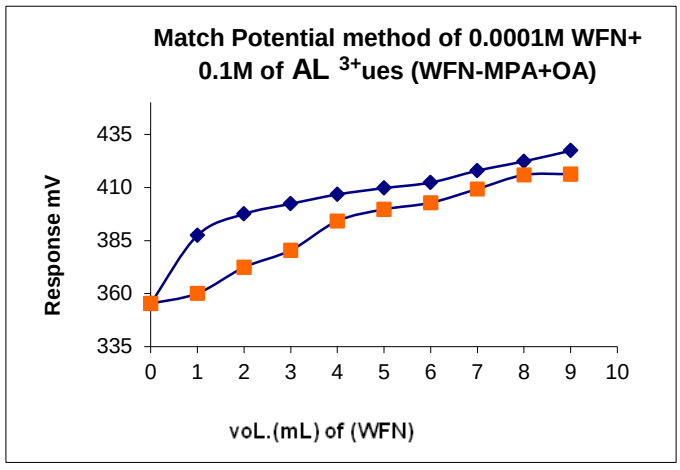

Match Potential method of 0.001M WFN+0.1M of K1+ ues (WFN-MPA+OA)
Response mV
445
420
395
370
0 1 2 3 4 5 6 7 8 9 10 11
voL.(mL) of (WFN)


Match Potential method of 0.0001M WFN+ 0.1M of K1+ ues (WFN-MPA+OA)
Response mV
430
400
370
340
0 1 2 3 4 5 6 7 8 9 10 11
voL.(mL)of (WFN)


Match Potential method of 0.001M WFN 0.1M of Ca2+ ues (WFN-MPA+OA)
Response mV
450
430
410
390
370
0 1 2 3 4 5 6 7 8 9 10 11
voL.(mL) of (WFN)


Match Potential method of 0.0001M WFN+ 0.1M of Ca2+ ues (WFN-MPA+OA)
Response mV
410
375
340
0 1 2 3 4 5 6 7 8 9 10 11
voL.(mL) of (WFN)


Match Potential method of 0.001M WFN+ 0.1M of Al3+ues (WFN-MPA+OA)
Response mV
440
405
370
0 1 2 3 4 5 6 7 8 9 10 11
voL.(mL) of (WFN)


Match Potential method of 0.0001M WFN+ 0.1M of AL 3+ues (WFN-MPA+OA)
Response mV
435
410
385
360
335
0 1 2 3 4 5 6 7 8 9 10
voL.(mL) of (WFN)

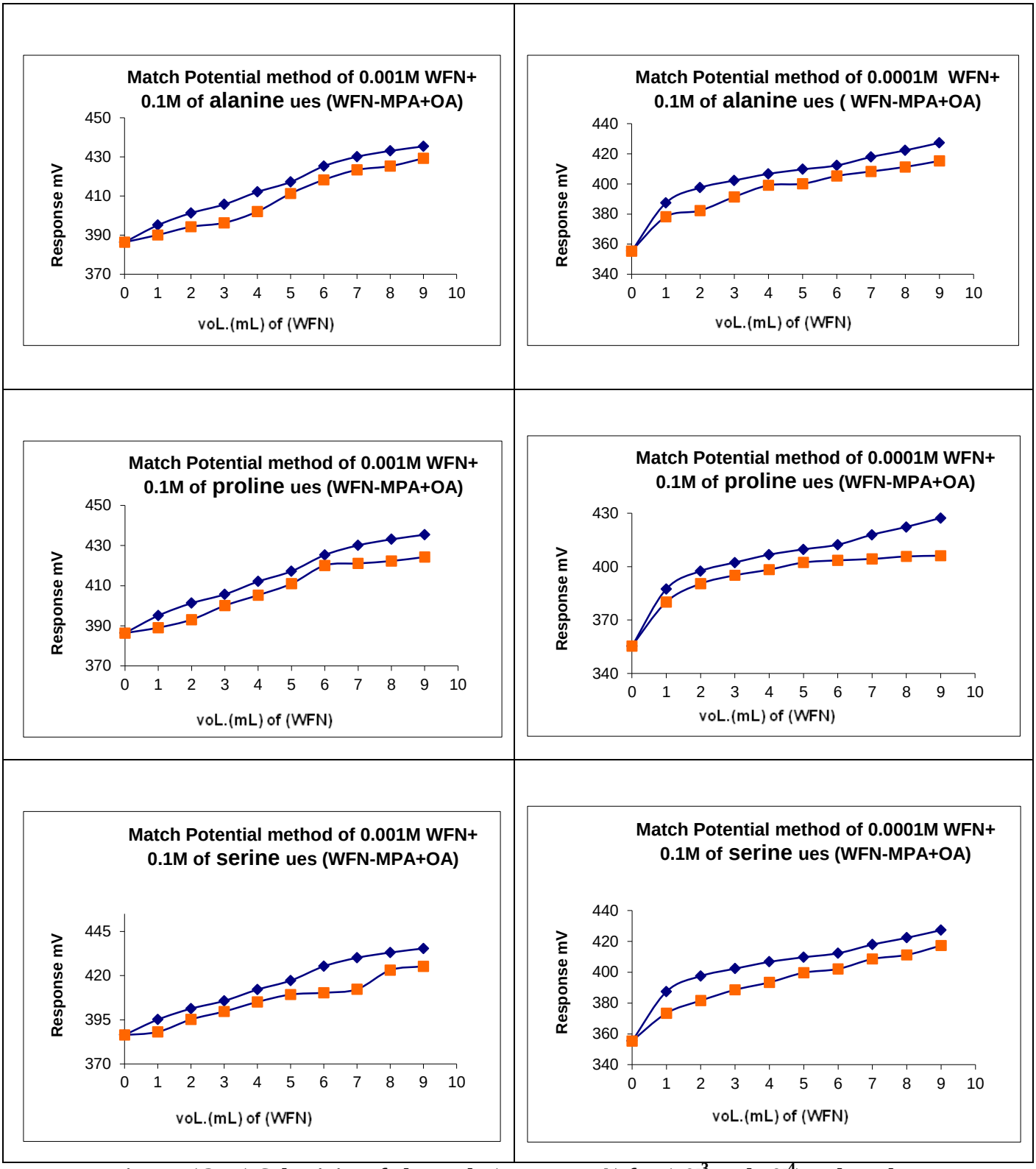
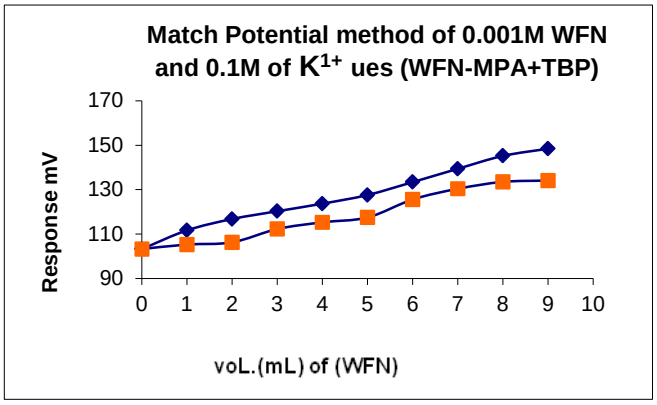
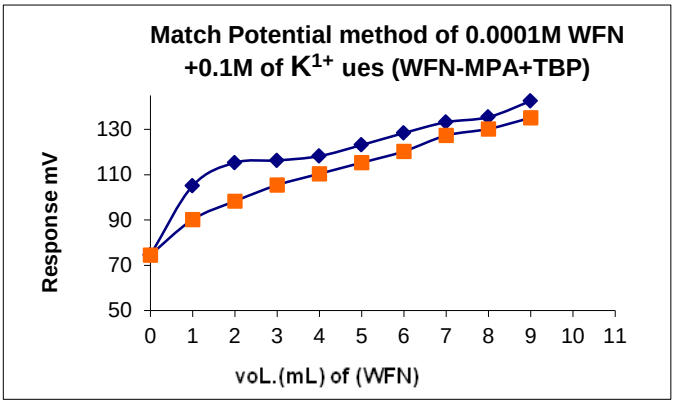
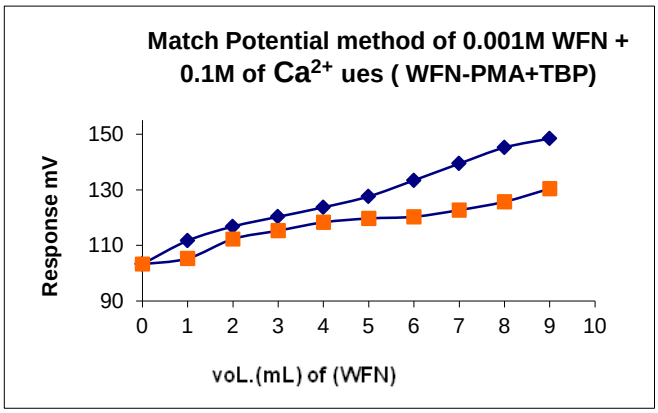
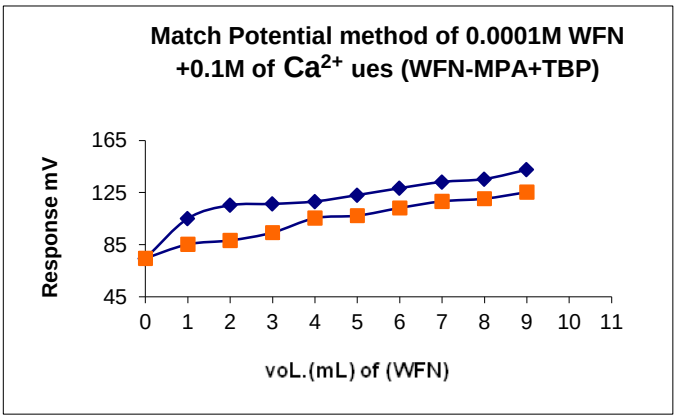


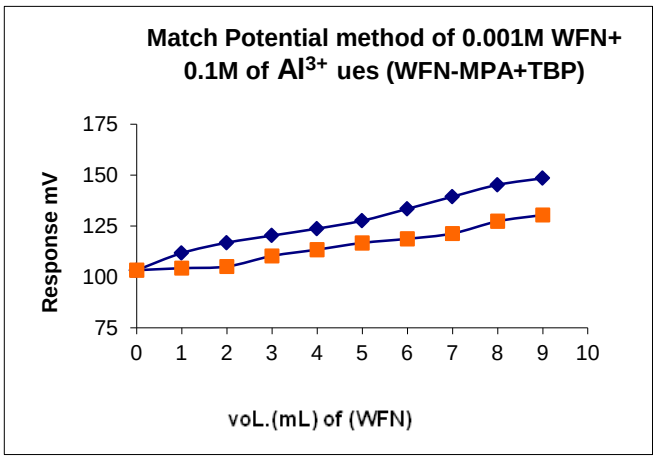
Figure. (3.17) Selectivity of electrode (WFN-MPA) for (10^{-3} and 10^{-4}) M based on OA , for cation and amino acid interfering by match potential method, ■ Solutions of interfering , ♦ WFN solutions.

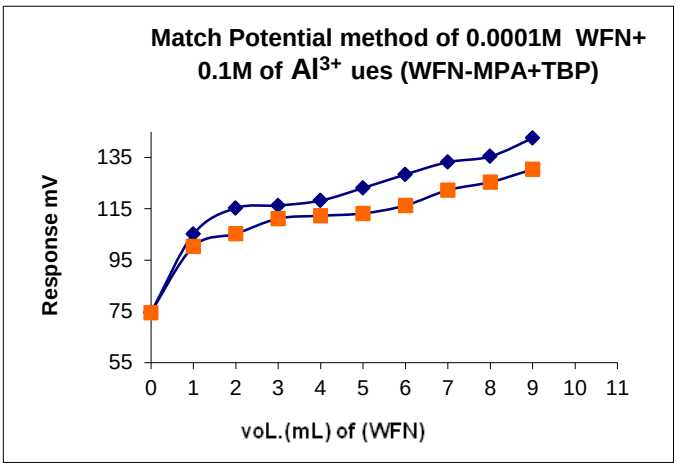

Match Potential method of 0.001M WFN and 0.1M of K1+ ues (WFN-MPA+TBP)
Response mV
170
150
130
110
90
0 1 2 3 4 5 6 7 8 9 10
voL.(mL) of (WFN)


Match Potential method of 0.0001M WFN +0.1M of K1+ ues (WFN-MPA+TBP)
Response mV
130
110
90
70
50
0 1 2 3 4 5 6 7 8 9 10 11
voL.(mL) of (WFN)


Match Potential method of 0.001M WFN + 0.1M of Ca2+ ues (WFN-PMA+TBP)
Response mV
150
130
110
90
0 1 2 3 4 5 6 7 8 9 10
voL.(mL) of (WFN)


Match Potential method of 0.0001M WFN +0.1M of Ca2+ ues (WFN-MPA+TBP)
Response mV
165
125
85
45
0 1 2 3 4 5 6 7 8 9 10 11
voL.(mL) of (WFN)


Match Potential method of 0.001M WFN+ 0.1M of Al3+ ues (WFN-MPA+TBP)
Response mV
175
150
125
100
75
0 1 2 3 4 5 6 7 8 9 10
voL.(mL) of (WFN)


Match Potential method of 0.0001M WFN+ 0.1M of Al3+ ues (WFN-MPA+TBP)
Response mV
135
115
95
75
55
0 1 2 3 4 5 6 7 8 9 10 11
voL.(mL) of (WFN)

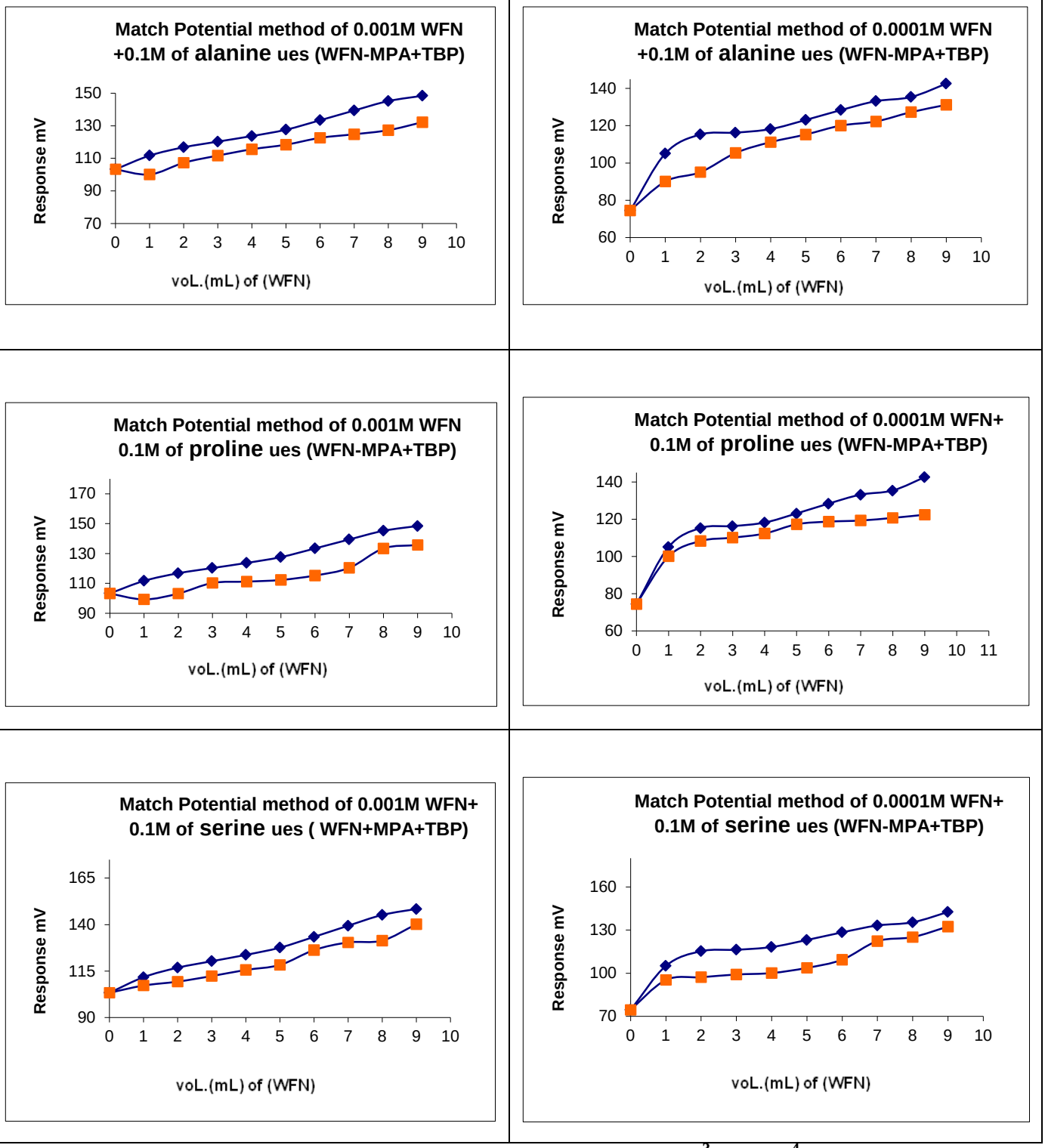
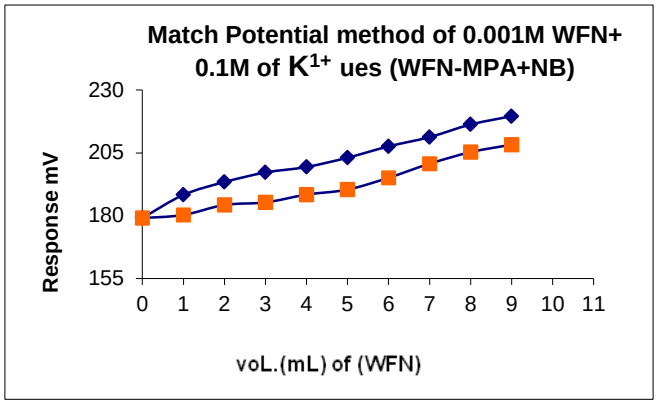
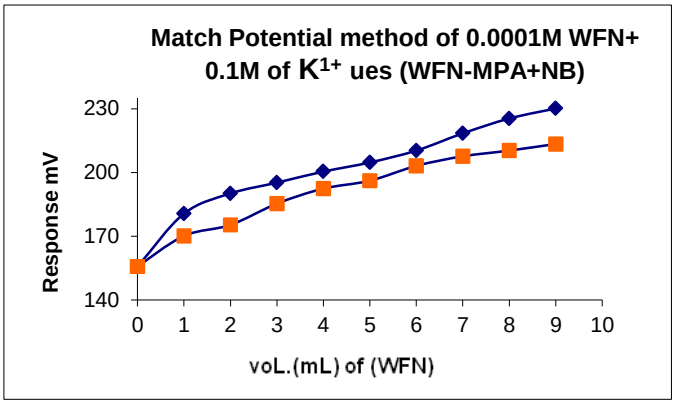
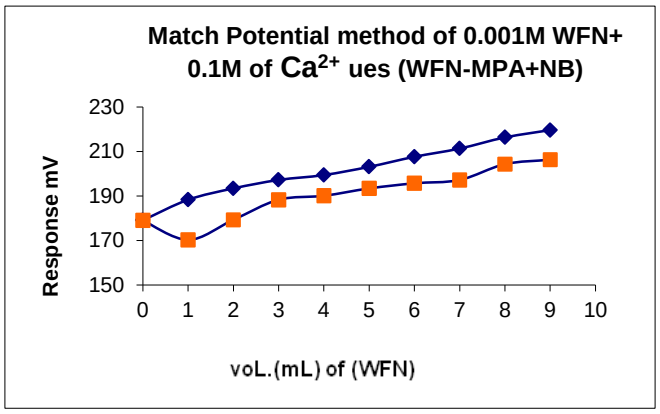
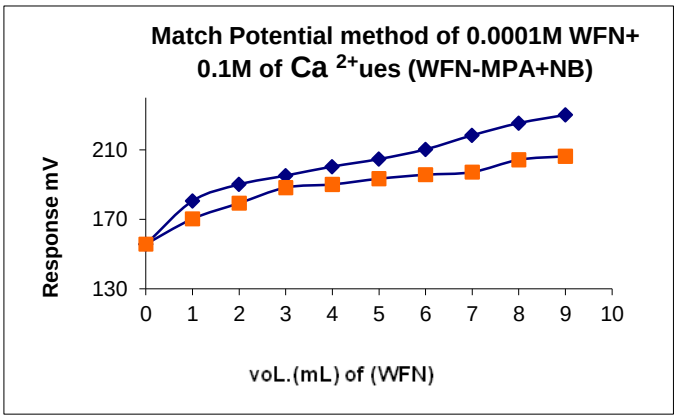


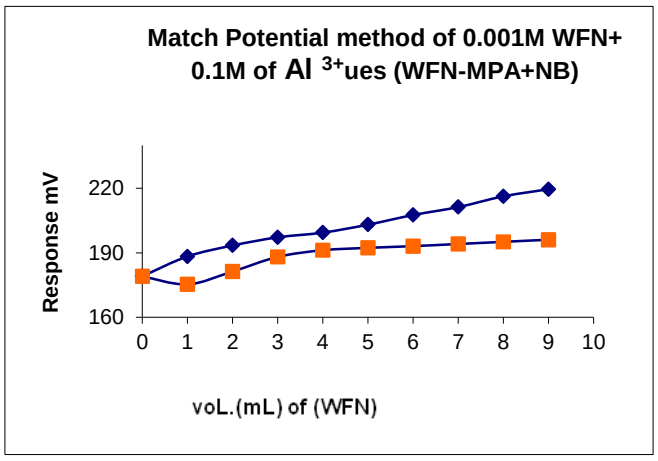
Figure (3.18) Selectivity of electrode (WFN-MPA) for (10^{-3} and 10^{-4}) M based on TBP , for cation and amino acid interfering by match potential method, ■ Solutions of interfering , ♦ WFN solutions.

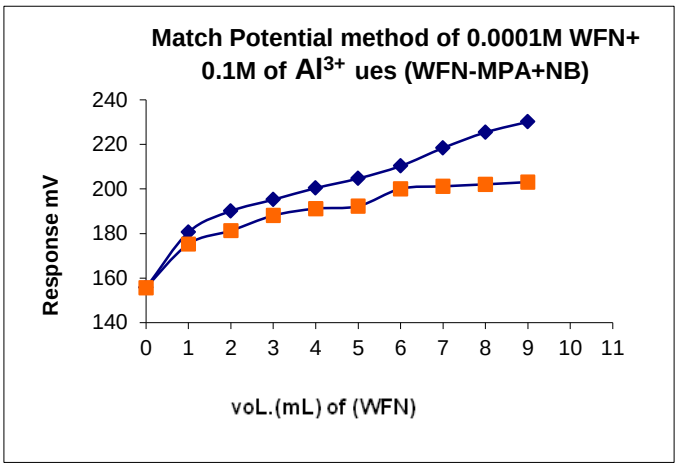

Match Potential method of 0.001M WFN+ 0.1M of K1+ ues (WFN-MPA+NB)
Response mV
230
205
180
155
0 1 2 3 4 5 6 7 8 9 10 11
voL.(mL) of (WFN)


Match Potential method of 0.0001M WFN+ 0.1M of K1+ ues (WFN-MPA+NB)
Response mV
230
200
170
140
0 1 2 3 4 5 6 7 8 9 10
voL.(mL) of (WFN)


Match Potential method of 0.001M WFN+ 0.1M of Ca2+ ues (WFN-MPA+NB)
Response mV
230
210
190
170
150
0 1 2 3 4 5 6 7 8 9 10
voL.(mL) of (WFN)


Match Potential method of 0.0001M WFN+ 0.1M of Ca 2+ues (WFN-MPA+NB)
Response mV
210
170
130
0 1 2 3 4 5 6 7 8 9 10
voL.(mL) of (WFN)


Match Potential method of 0.001M WFN+ 0.1M of Al 3+ues (WFN-MPA+NB)
Response mV
220
190
160
0 1 2 3 4 5 6 7 8 9 10
voL.(mL) of (WFN)


Match Potential method of 0.0001M WFN+ 0.1M of Al3+ ues (WFN-MPA+NB)
Response mV
240
220
200
180
160
140
0 1 2 3 4 5 6 7 8 9 10 11
voL.(mL) of (WFN)

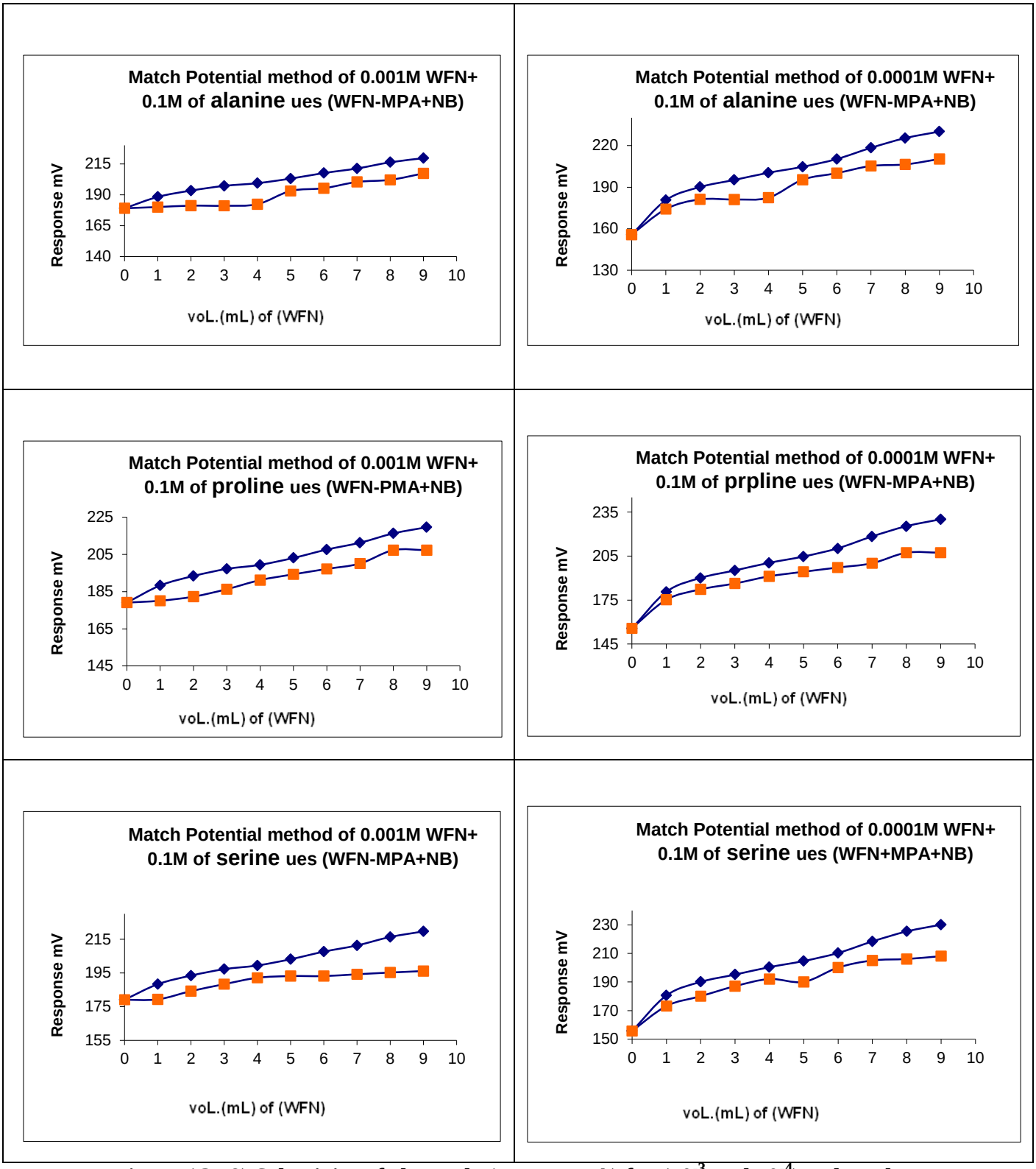
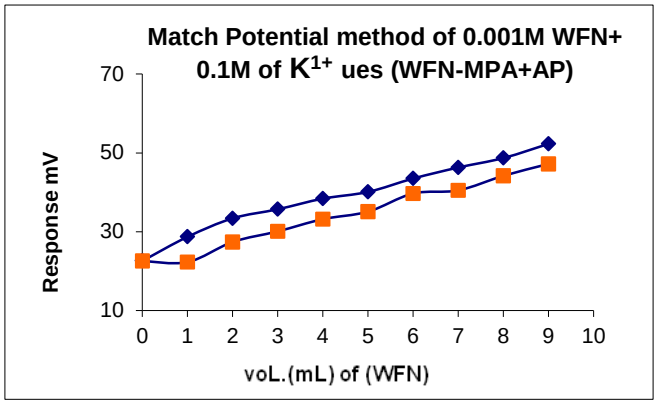
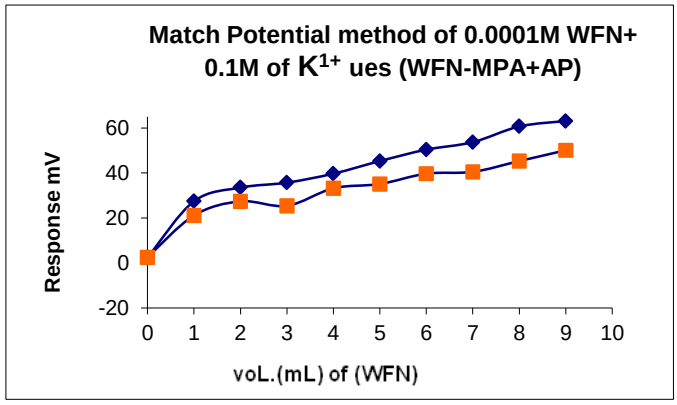
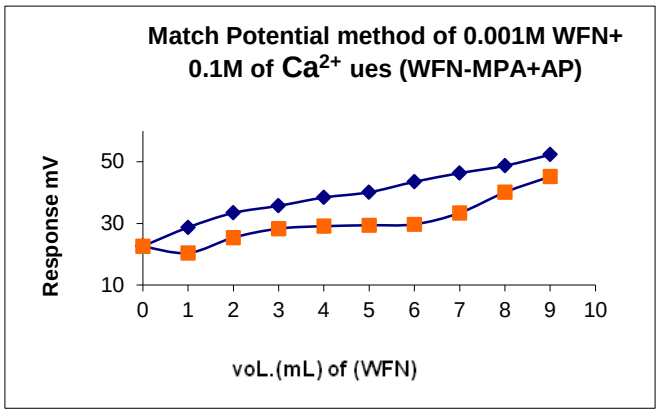
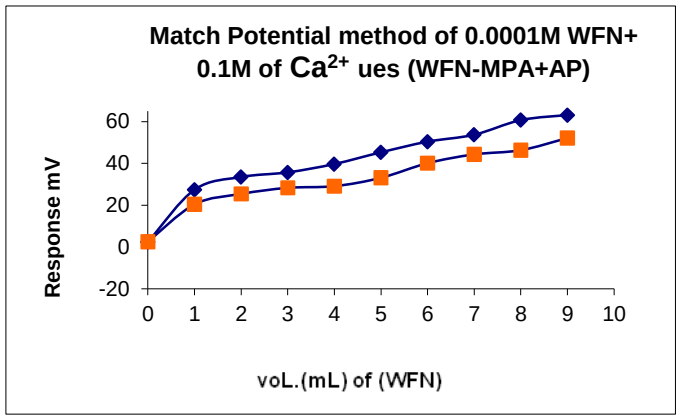


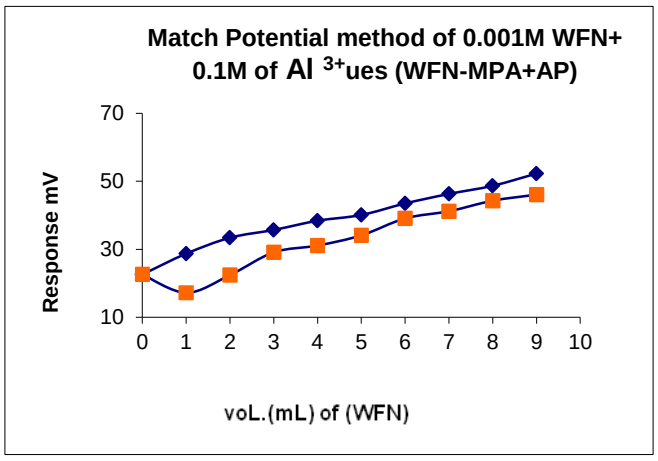
Figure (3.19) Selectivity of electrode (WFN-MPA) for (10^{-3} and 10^{-4}) M based on NB , for cation and amino acid interfering by match potential method, ■ Solutions of interfering , ♦ WFN solutions.

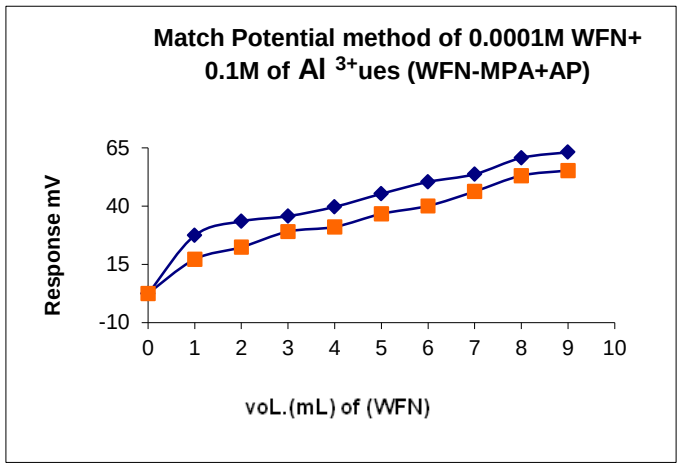

Match Potential method of 0.001M WFN+ 0.1M of K1+ ues (WFN-MPA+AP)
Response mV
70
50
30
10
0 1 2 3 4 5 6 7 8 9 10
voL.(mL) of (WFN)


Match Potential method of 0.0001M WFN+ 0.1M of K1+ ues (WFN-MPA+AP)
Response mV
60
40
20
0
-20
0 1 2 3 4 5 6 7 8 9 10
voL.(mL) of (WFN)


Match Potential method of 0.001M WFN+ 0.1M of Ca2+ ues (WFN-MPA+AP)
Response mV
50
30
10
0 1 2 3 4 5 6 7 8 9 10
voL.(mL) of (WFN)


Match Potential method of 0.0001M WFN+ 0.1M of Ca2+ ues (WFN-MPA+AP)
Response mV
60
40
20
0
-20
0 1 2 3 4 5 6 7 8 9 10
voL.(mL) of (WFN)


Match Potential method of 0.001M WFN+ 0.1M of Al 3+ues (WFN-MPA+AP)
Response mV
70
50
30
10
0 1 2 3 4 5 6 7 8 9 10
voL.(mL) of (WFN)


Match Potential method of 0.0001M WFN+ 0.1M of Al 3+ues (WFN-MPA+AP)
Response mV
65
40
15
-10
0 1 2 3 4 5 6 7 8 9 10
voL.(mL) of (WFN)

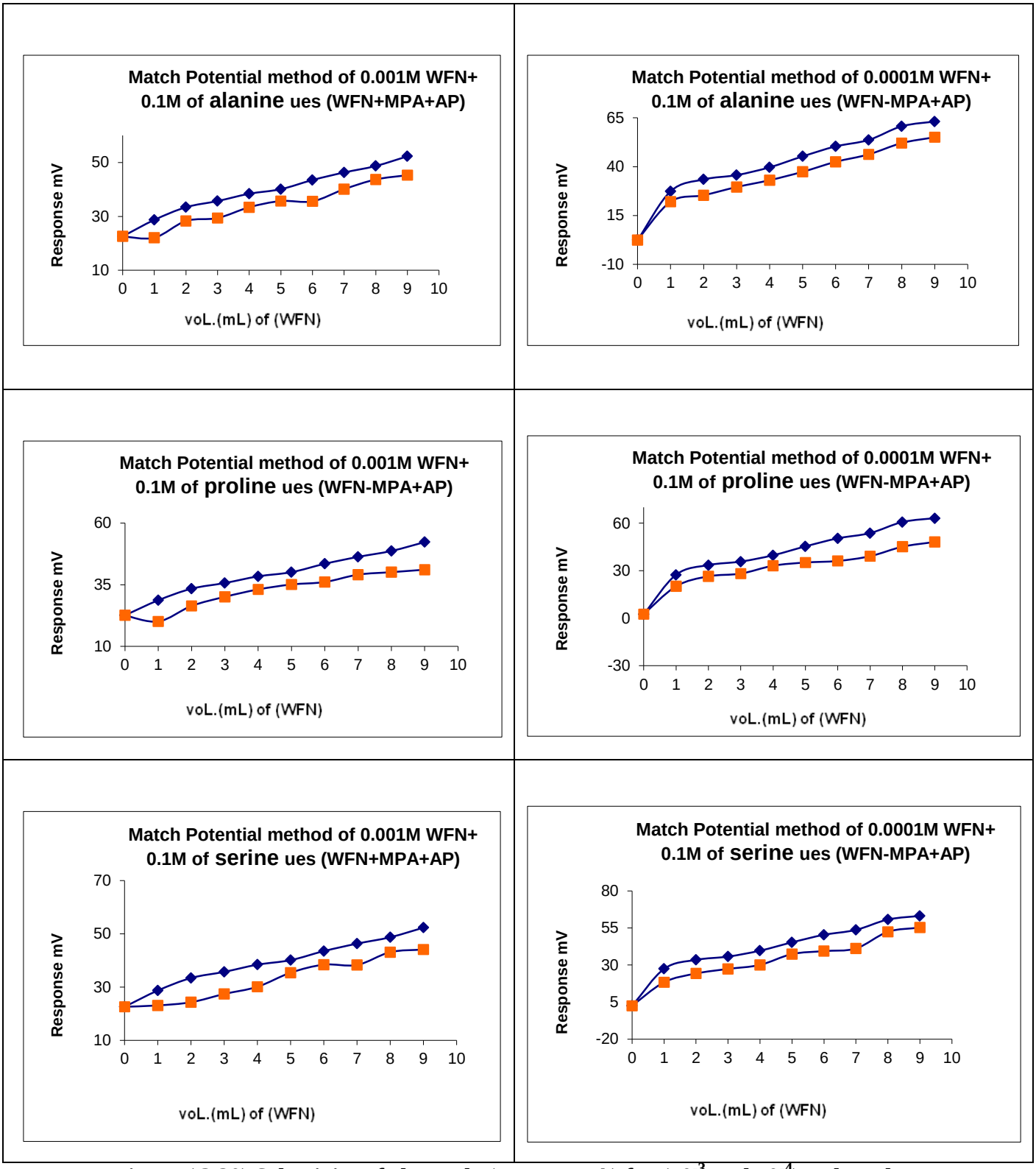
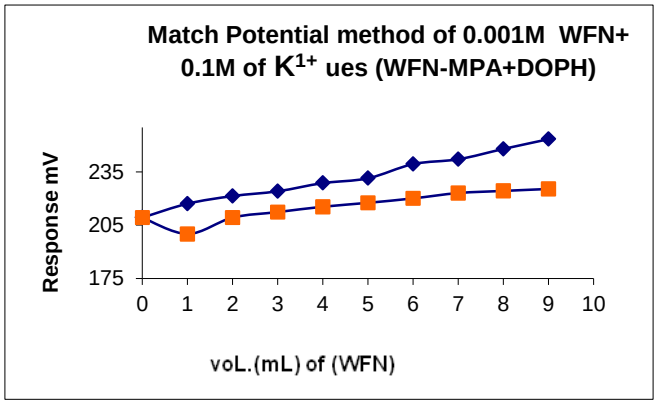
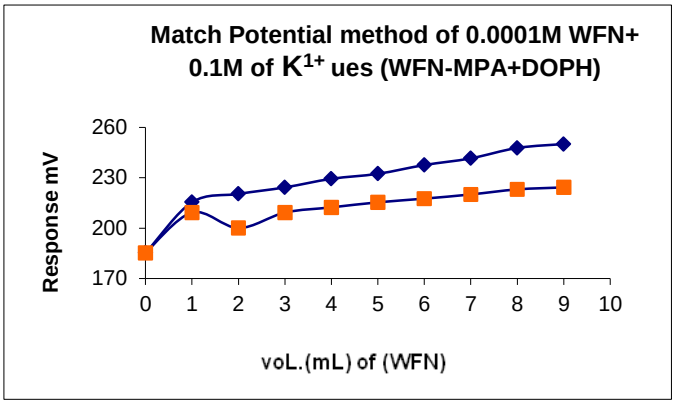
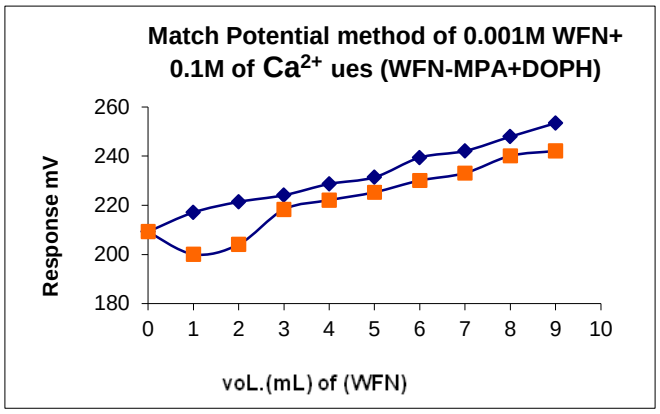
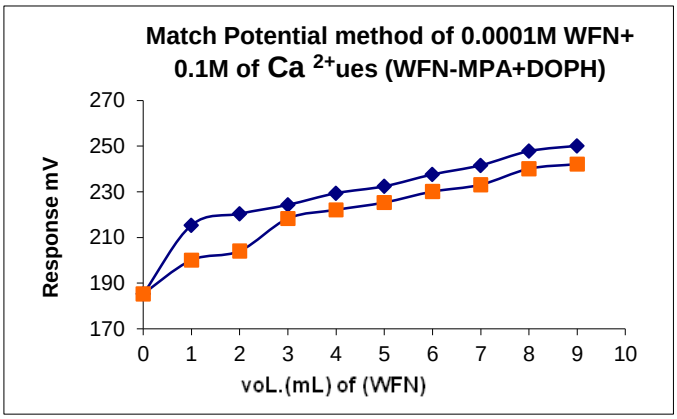


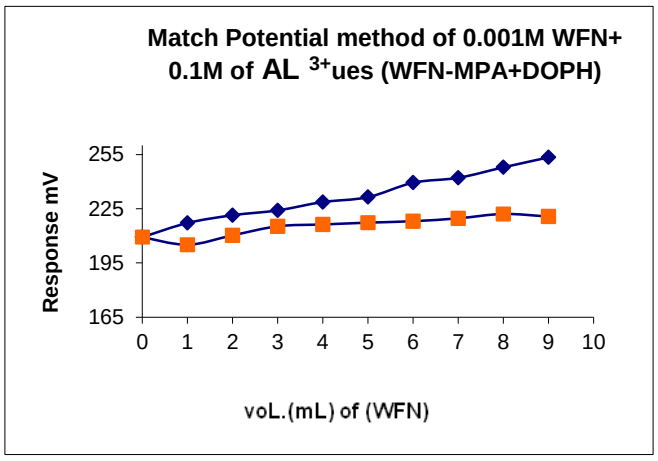
Figure (3.20) Selectivity of electrode (WFN-MPA) for (10^{-3} and 10^{-4}) M based on AP , for cation and amino acid interfering by match potential method, ■ Solutions of interfering , ♦ WFN solutions.

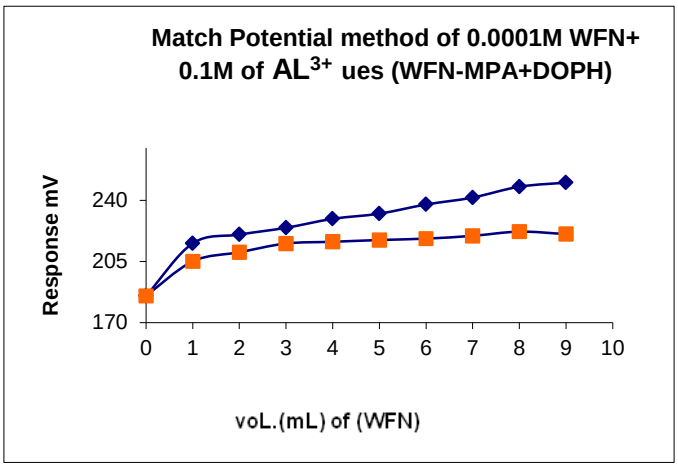

Match Potential method of 0.001M WFN+ 0.1M of K1+ ues (WFN-MPA+DOPH)
Response mV
235
205
175
0 1 2 3 4 5 6 7 8 9 10
voL.(mL) of (WFN)


Match Potential method of 0.0001M WFN+ 0.1M of K1+ ues (WFN-MPA+DOPH)
Response mV
260
230
200
170
0 1 2 3 4 5 6 7 8 9 10
voL.(mL) of (WFN)


Match Potential method of 0.001M WFN+ 0.1M of Ca2+ ues (WFN-MPA+DOPH)
Response mV
260
240
220
200
180
0 1 2 3 4 5 6 7 8 9 10
voL.(mL) of (WFN)


Match Potential method of 0.0001M WFN+ 0.1M of Ca 2+ues (WFN-MPA+DOPH)
Response mV
270
250
230
210
190
170
0 1 2 3 4 5 6 7 8 9 10
voL.(mL) of (WFN)


Match Potential method of 0.001M WFN+ 0.1M of AL 3+ues (WFN-MPA+DOPH)
Response mV
255
225
195
165
0 1 2 3 4 5 6 7 8 9 10
voL.(mL) of (WFN)


Match Potential method of 0.0001M WFN+ 0.1M of AL3+ ues (WFN-MPA+DOPH)
Response mV
240
205
170
0 1 2 3 4 5 6 7 8 9 10
voL.(mL) of (WFN)

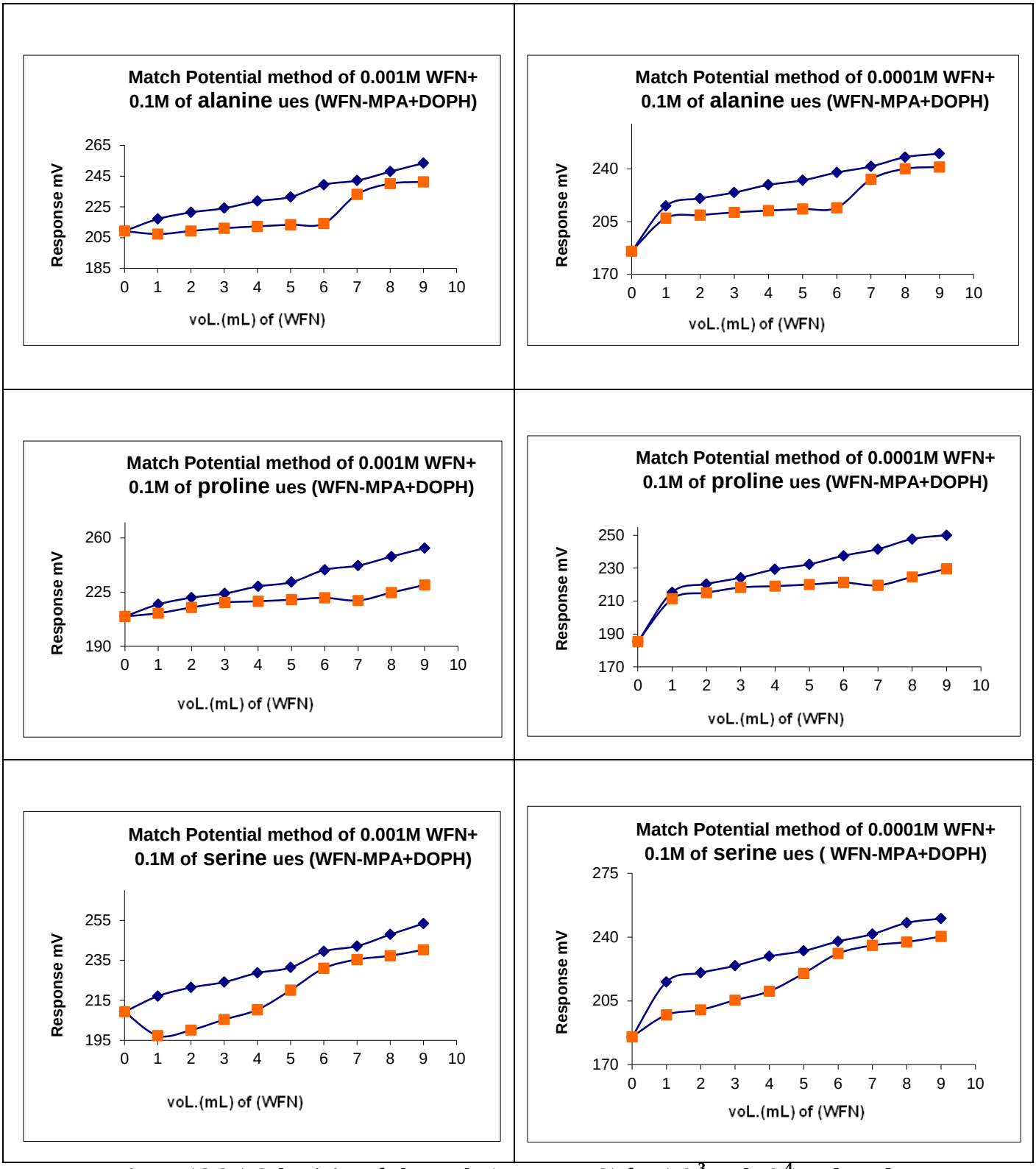
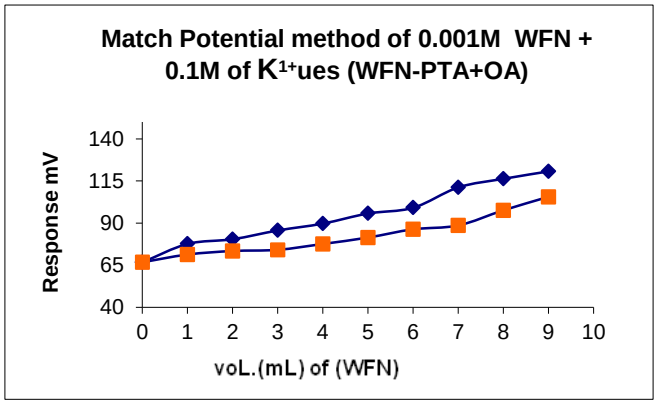
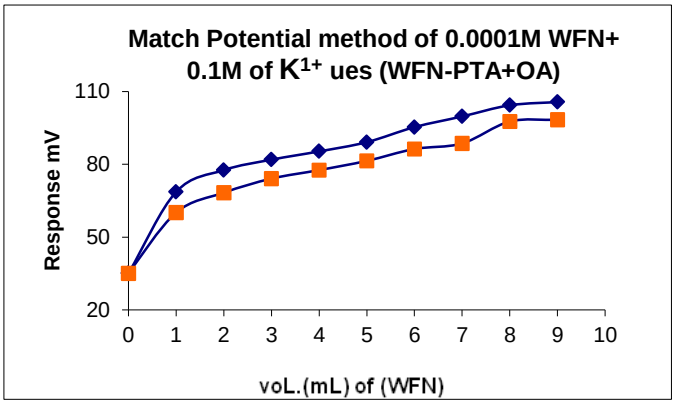
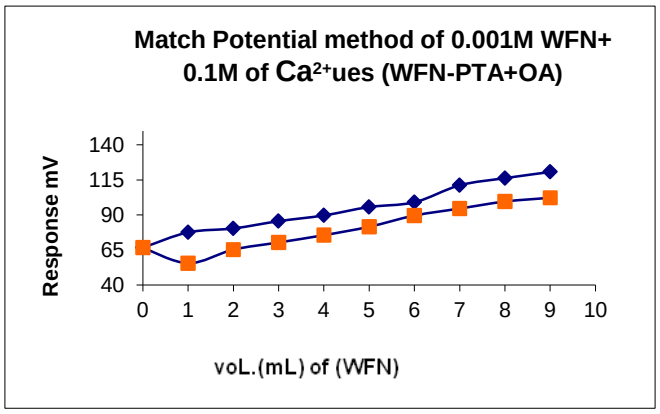
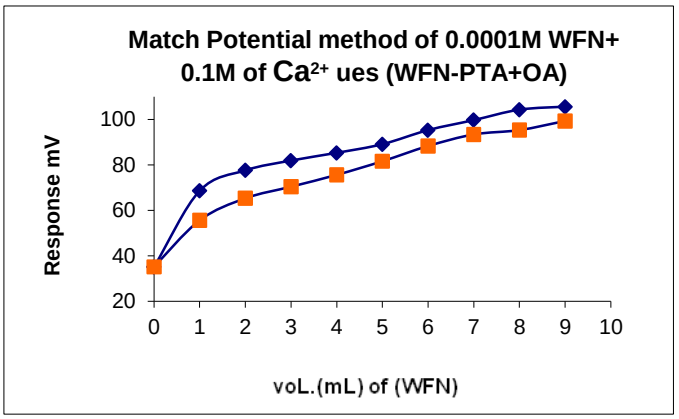


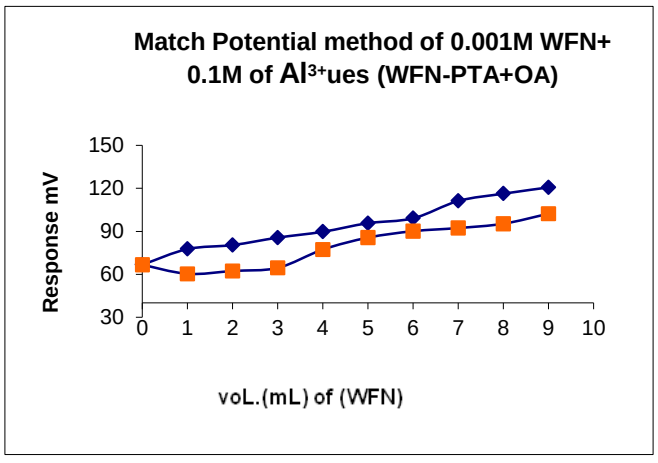
Figure (3.21) Selectivity of electrode (WFN-MPA) for (10^{-3} and 10^{-4}) M based on DOPH, for cation and amino acid interfering by match potential method, ■ Solutions of interfering , ♦ WFN solutions.

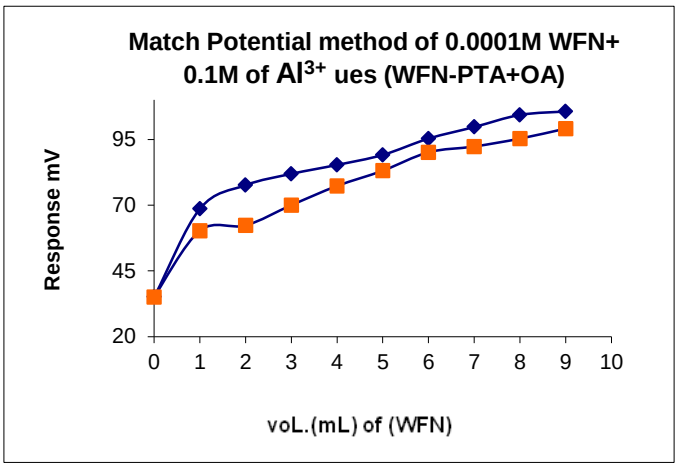

Match Potential method of 0.001M WFN + 0.1M of K1+ues (WFN-PTA+OA)
Response mV
140
115
90
65
40
0 1 2 3 4 5 6 7 8 9 10
voL.(mL) of (WFN)


Match Potential method of 0.0001M WFN+ 0.1M of K1+ ues (WFN-PTA+OA)
Response mV
110
80
50
20
0 1 2 3 4 5 6 7 8 9 10
voL.(mL) of (WFN)


Match Potential method of 0.001M WFN+ 0.1M of Ca2+ues (WFN-PTA+OA)
Response mV
140
115
90
65
40
0 1 2 3 4 5 6 7 8 9 10
voL.(mL) of (WFN)


Match Potential method of 0.0001M WFN+ 0.1M of Ca2+ ues (WFN-PTA+OA)
Response mV
100
80
60
40
20
0 1 2 3 4 5 6 7 8 9 10
voL.(mL) of (WFN)


Match Potential method of 0.001M WFN+ 0.1M of Al3+ues (WFN-PTA+OA)
Response mV
150
120
90
60
30
0 1 2 3 4 5 6 7 8 9 10
voL.(mL) of (WFN)


Match Potential method of 0.0001M WFN+ 0.1M of Al3+ ues (WFN-PTA+OA)
Response mV
95
70
45
20
0 1 2 3 4 5 6 7 8 9 10
voL.(mL) of (WFN)

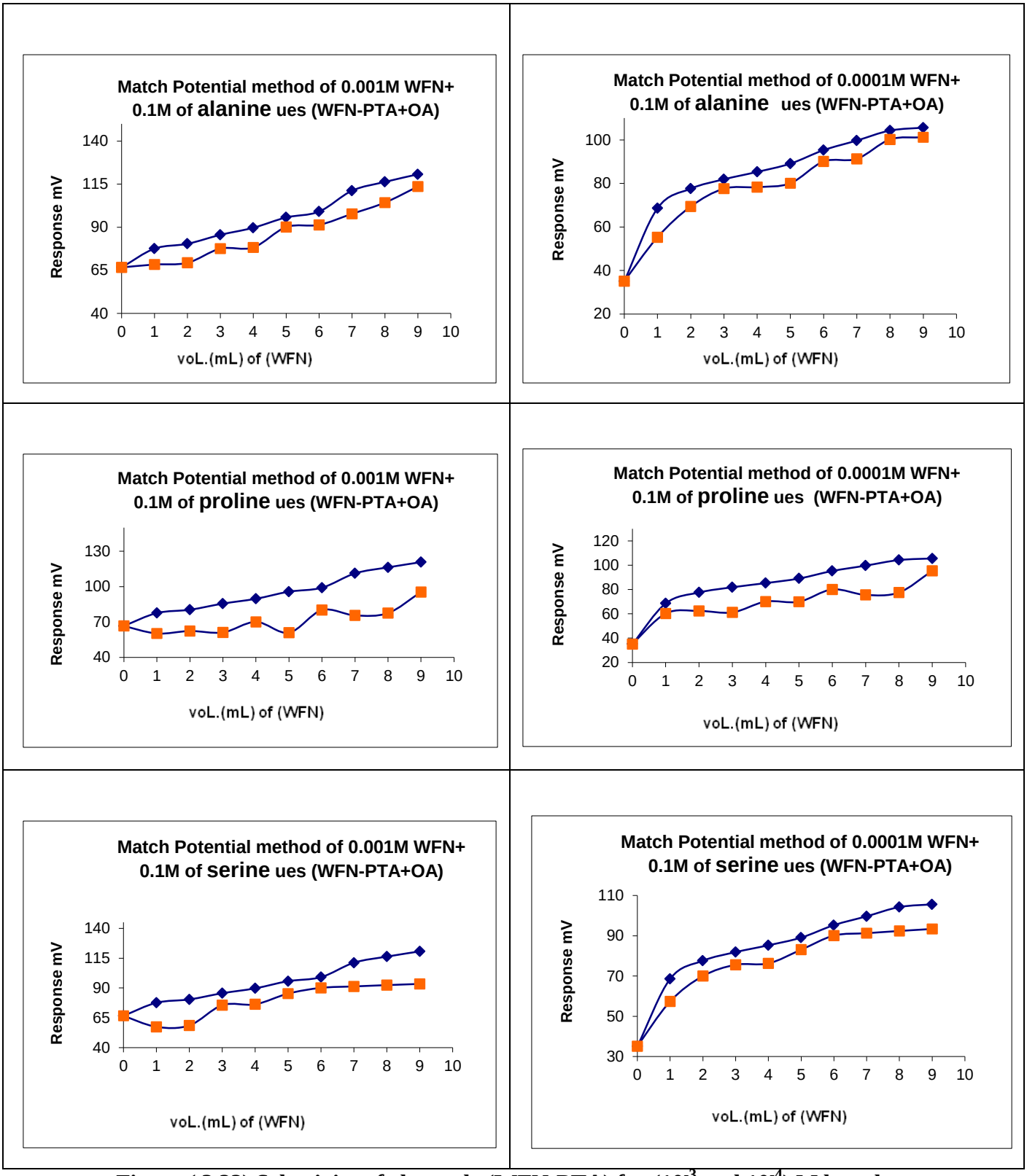
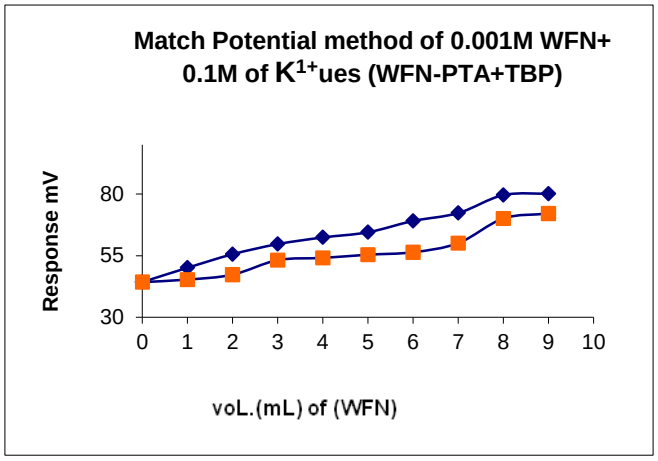
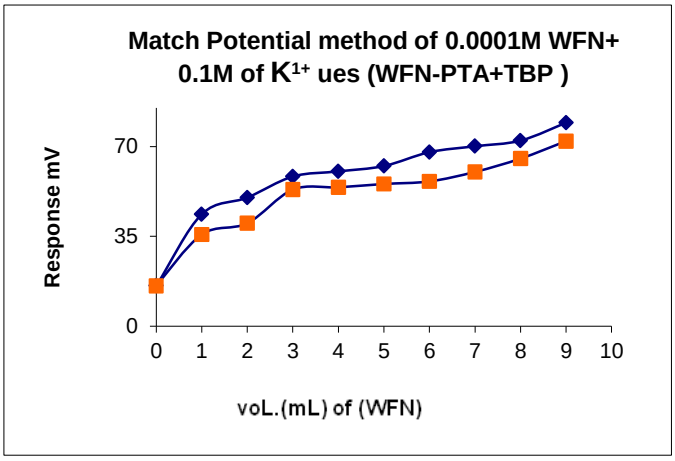
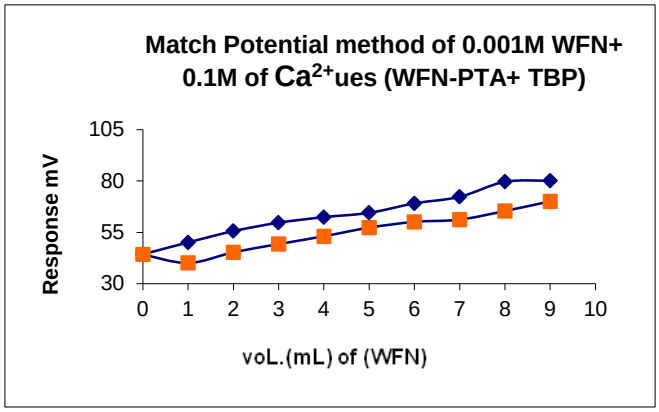
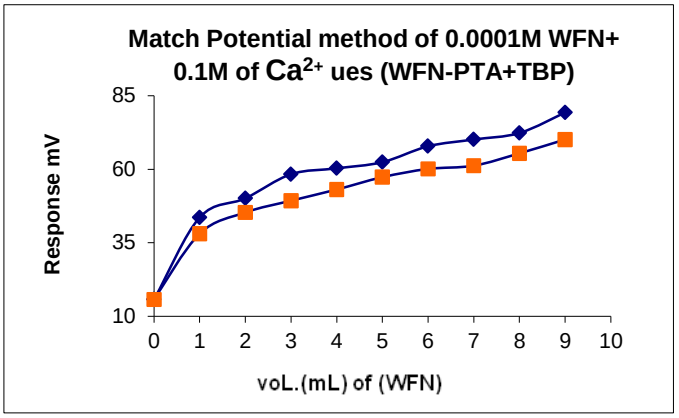


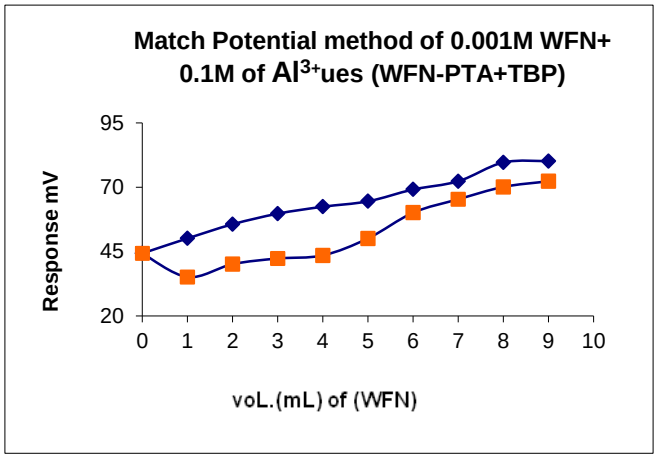
Figure (3.22) Selectivity of electrode (WFN-PTA) for (10^{-3} and 10^{-4}) M based on OA, for cation and amino acid interfering by match potential method, ■ Solutions of interfering , ♦ WFN solutions.

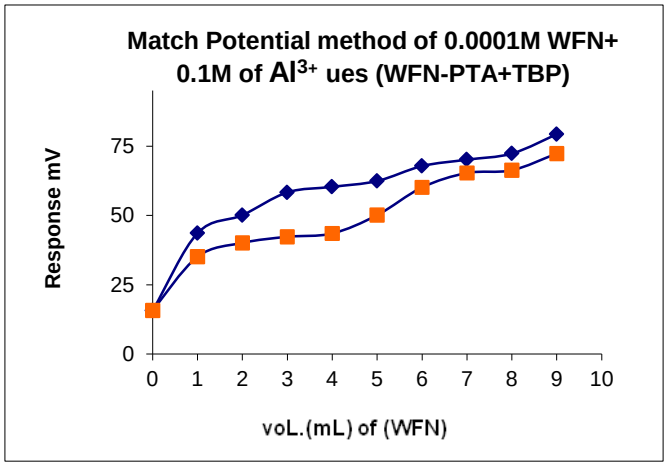

Match Potential method of 0.001M WFN+ 0.1M of K1+ues (WFN-PTA+TBP)
Response mV
80
55
30
0 1 2 3 4 5 6 7 8 9 10
voL.(mL) of (WFN)


Match Potential method of 0.0001M WFN+ 0.1M of K1+ ues (WFN-PTA+TBP)
Response mV
70
35
0
0 1 2 3 4 5 6 7 8 9 10
voL.(mL) of (WFN)


Match Potential method of 0.001M WFN+ 0.1M of Ca2+ues (WFN-PTA+ TBP)
Response mV
105
80
55
30
0 1 2 3 4 5 6 7 8 9 10
voL.(mL) of (WFN)


Match Potential method of 0.0001M WFN+ 0.1M of Ca2+ ues (WFN-PTA+TBP)
Response mV
85
60
35
10
0 1 2 3 4 5 6 7 8 9 10
voL.(mL) of (WFN)


Match Potential method of 0.001M WFN+ 0.1M of Al3+ues (WFN-PTA+TBP)
Response mV
95
70
45
20
0 1 2 3 4 5 6 7 8 9 10
voL.(mL) of (WFN)


Match Potential method of 0.0001M WFN+ 0.1M of Al3+ ues (WFN-PTA+TBP)
Response mV
75
50
25
0
0 1 2 3 4 5 6 7 8 9 10
voL.(mL) of (WFN)

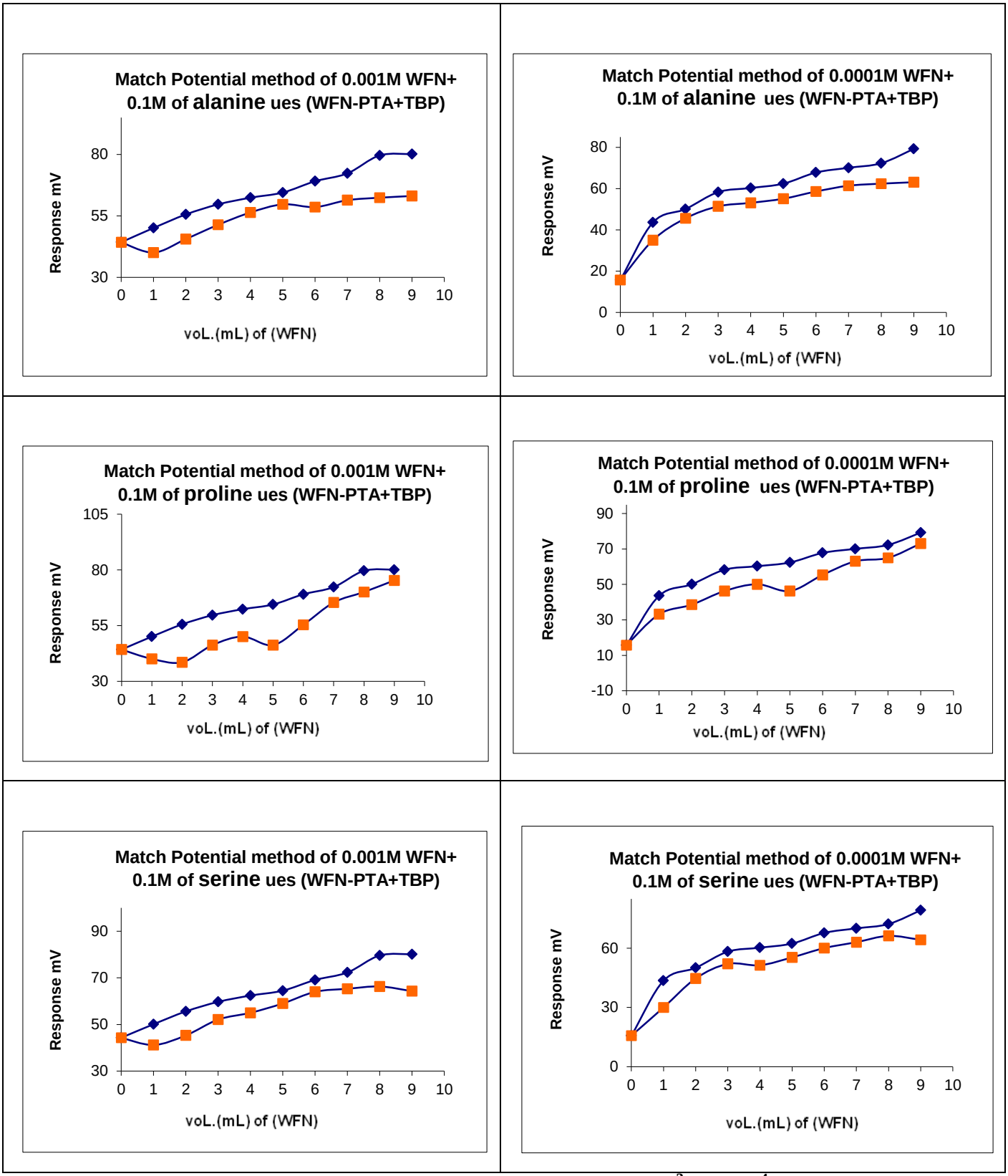
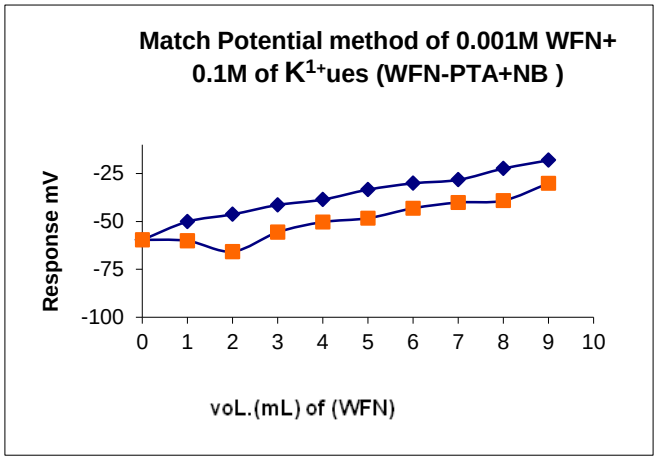
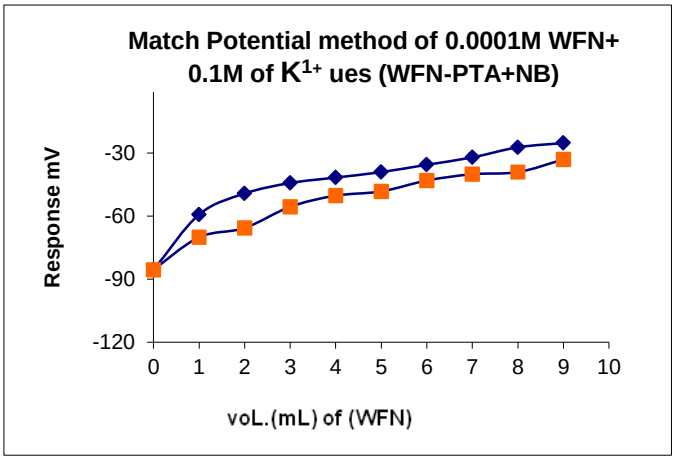
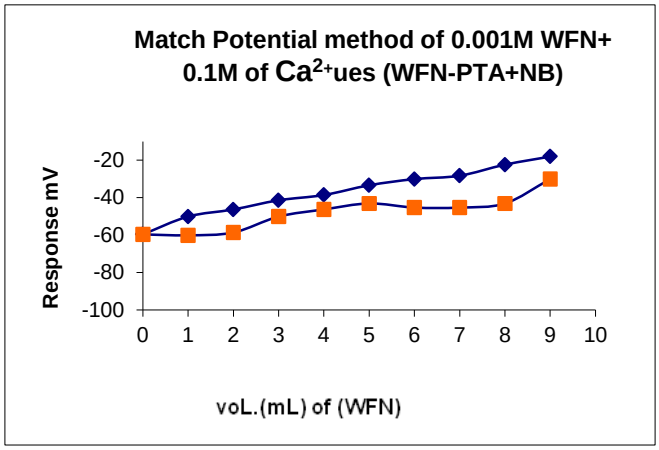
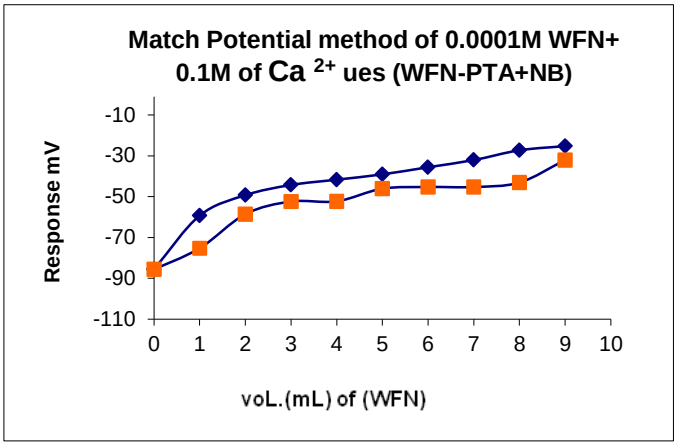


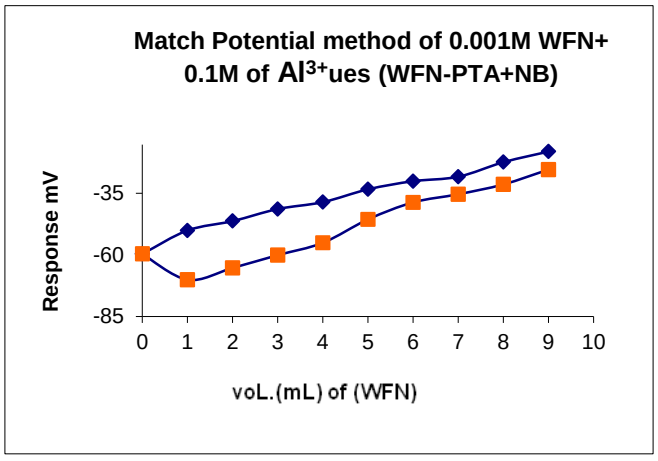
Figure (3.23) Selectivity of electrode (WFN-PTA) for (10^{-3} and 10^{-4}) M based on TBP, for cation and amino acid interfering by match potential method, ■ Solutions of interfering , ♦ WFN solutions.

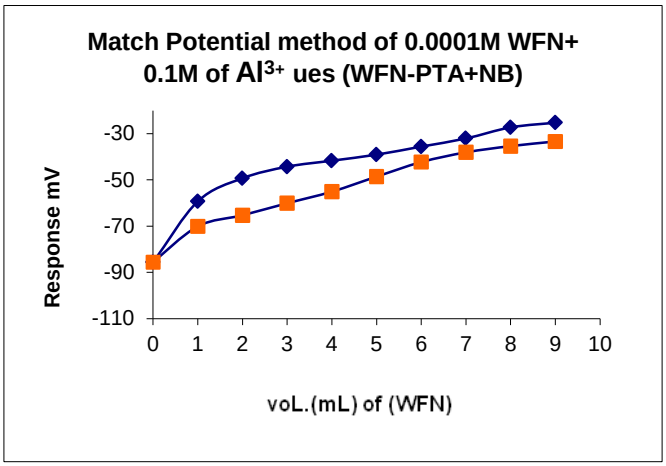

Match Potential method of 0.001M WFN+ 0.1M of K1+ues (WFN-PTA+NB)
Response mV
-25
-50
-75
-100
0 1 2 3 4 5 6 7 8 9 10
voL.(mL) of (WFN)


Match Potential method of 0.0001M WFN+ 0.1M of K1+ ues (WFN-PTA+NB)
Response mV
-30
-60
-90
-120
0 1 2 3 4 5 6 7 8 9 10
voL.(mL) of (WFN)


Match Potential method of 0.001M WFN+ 0.1M of Ca2+ues (WFN-PTA+NB)
Response mV
-20
-40
-60
-80
-100
0 1 2 3 4 5 6 7 8 9 10
voL.(mL) of (WFN)


Match Potential method of 0.0001M WFN+ 0.1M of Ca 2+ ues (WFN-PTA+NB)
Response mV
-10
-30
-50
-70
-90
-110
0 1 2 3 4 5 6 7 8 9 10
voL.(mL) of (WFN)


Match Potential method of 0.001M WFN+ 0.1M of Al3+ues (WFN-PTA+NB)
Response mV
-35
-60
-85
0 1 2 3 4 5 6 7 8 9 10
voL.(mL) of (WFN)


Match Potential method of 0.0001M WFN+ 0.1M of Al3+ ues (WFN-PTA+NB)
Response mV
-30
-50
-70
-90
-110
0 1 2 3 4 5 6 7 8 9 10
voL.(mL) of (WFN)

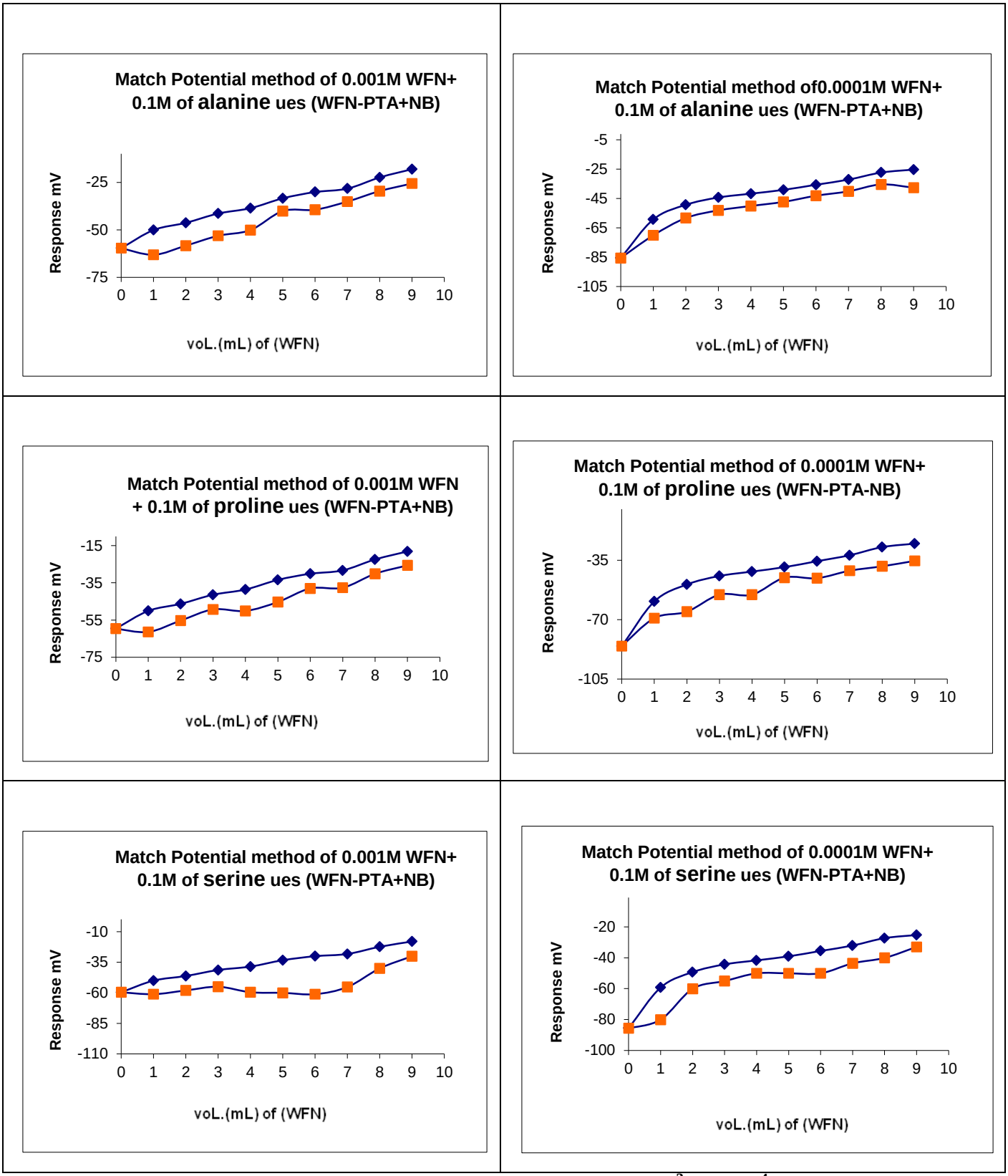
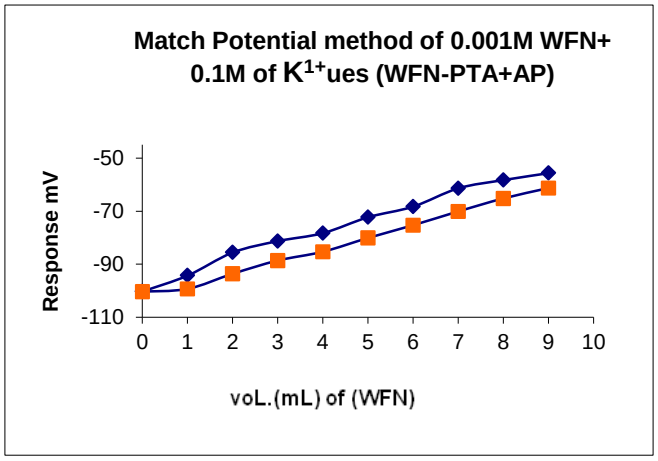
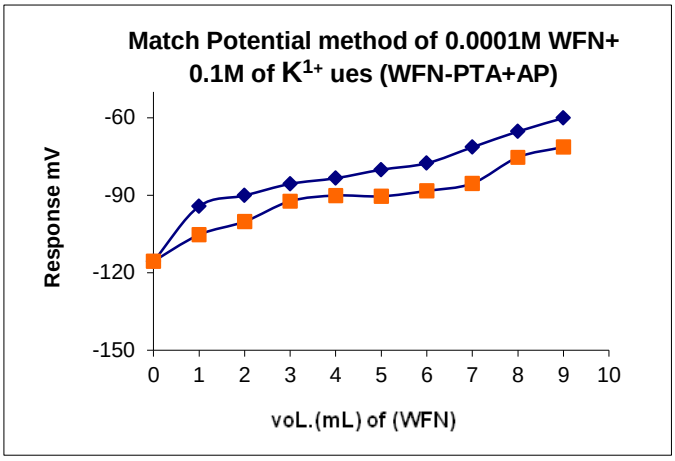
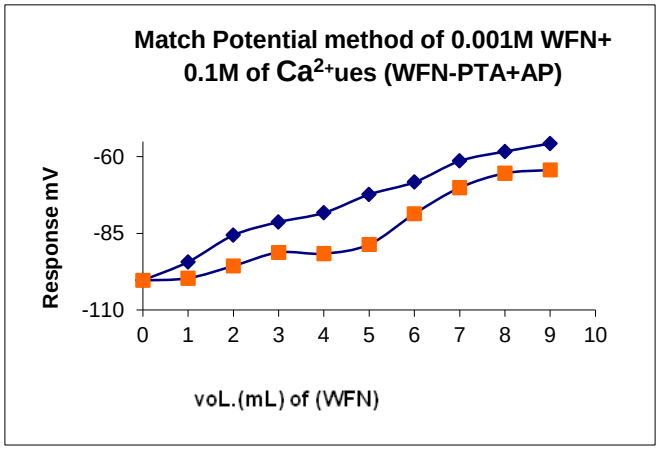
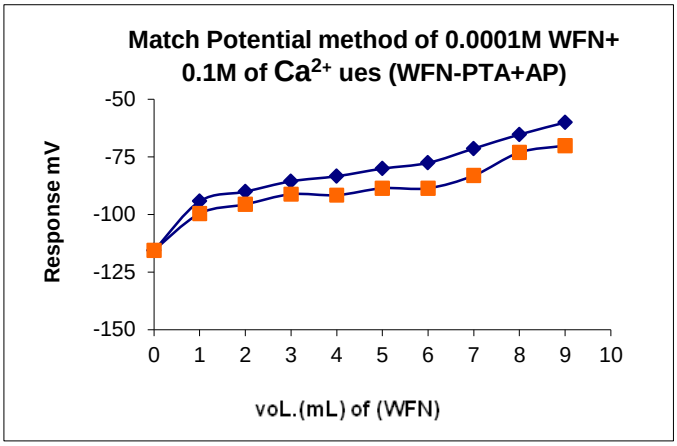


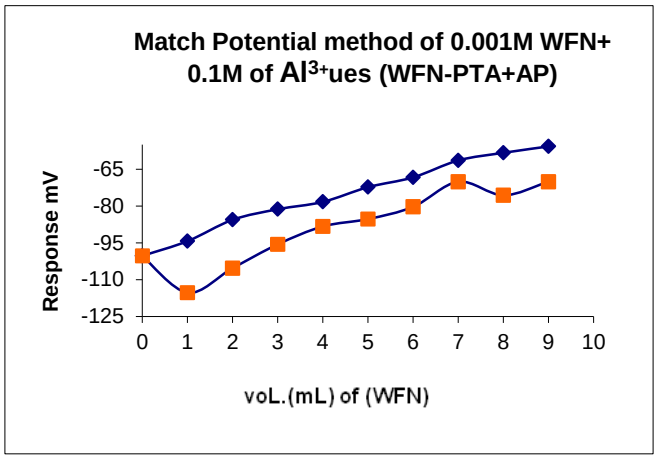
Figure (3.24) Selectivity of electrode (WFN-PTA) for (10^{-3} and 10^{-4}) M based on NB, for cation and amino acid interfering by match potential method, ■ Solutions of interfering , ♦ WFN solutions.

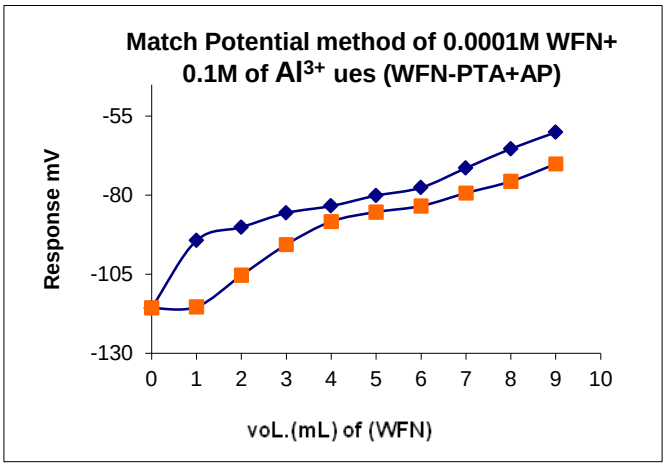

Match Potential method of 0.001M WFN+ 0.1M of K1+ues (WFN-PTA+AP)
Response mV
-50
-70
-90
-110
0 1 2 3 4 5 6 7 8 9 10
voL.(mL) of (WFN)


Match Potential method of 0.0001M WFN+ 0.1M of K1+ ues (WFN-PTA+AP)
Response mV
-60
-90
-120
-150
0 1 2 3 4 5 6 7 8 9 10
voL.(mL) of (WFN)


Match Potential method of 0.001M WFN+ 0.1M of Ca2+ues (WFN-PTA+AP)
Response mV
-60
-85
-110
0 1 2 3 4 5 6 7 8 9 10
voL.(mL) of (WFN)


Match Potential method of 0.0001M WFN+ 0.1M of Ca2+ ues (WFN-PTA+AP)
Response mV
-50
-75
-100
-125
-150
0 1 2 3 4 5 6 7 8 9 10
voL.(mL) of (WFN)


Match Potential method of 0.001M WFN+ 0.1M of Al3+ues (WFN-PTA+AP)
Response mV
-65
-80
-95
-110
-125
0 1 2 3 4 5 6 7 8 9 10
voL.(mL) of (WFN)


Match Potential method of 0.0001M WFN+ 0.1M of Al3+ ues (WFN-PTA+AP)
Response mV
-55
-80
-105
-130
0 1 2 3 4 5 6 7 8 9 10
voL.(mL) of (WFN)

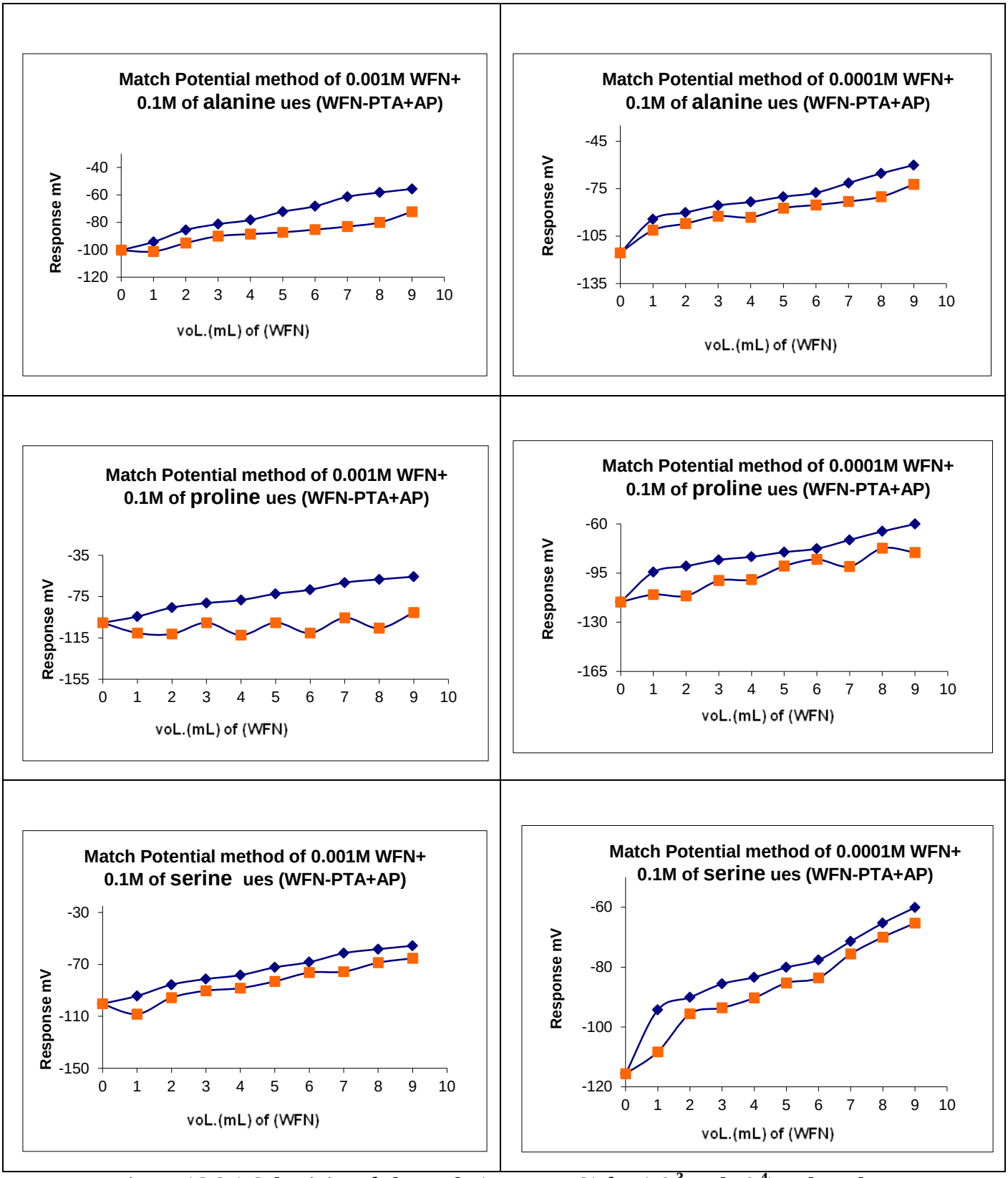
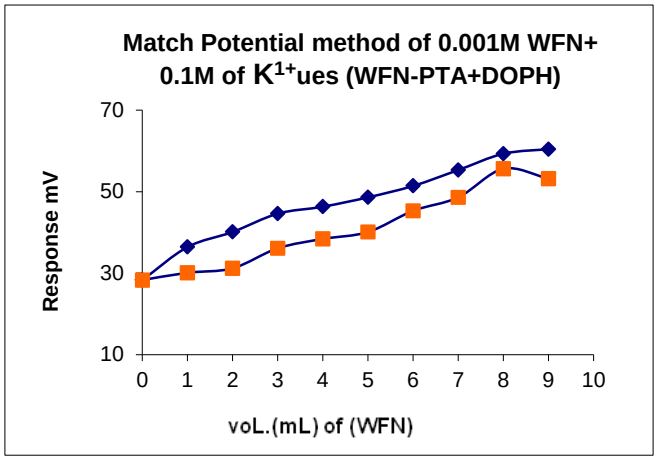
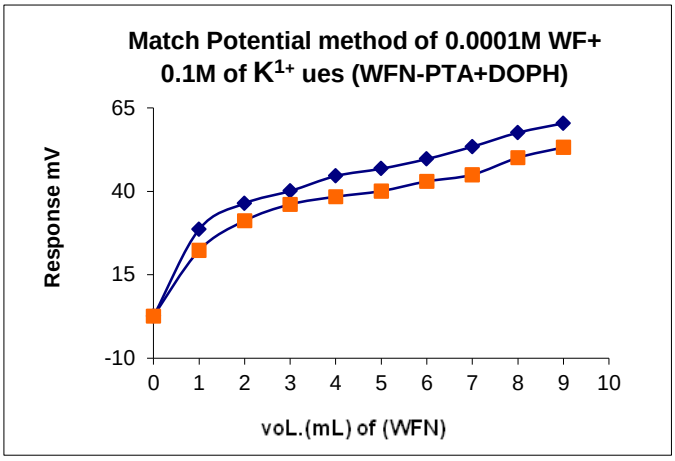
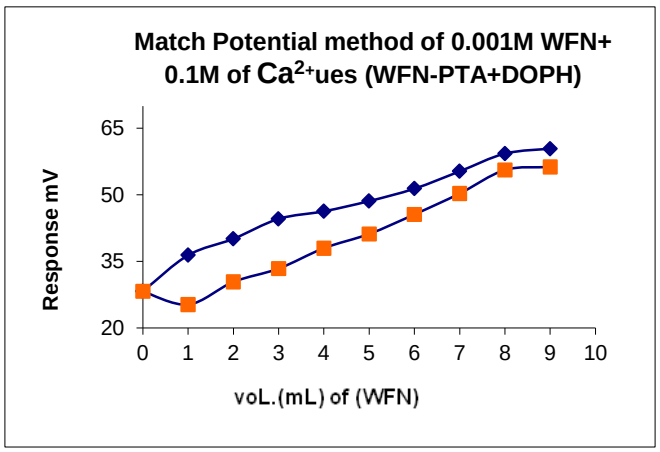
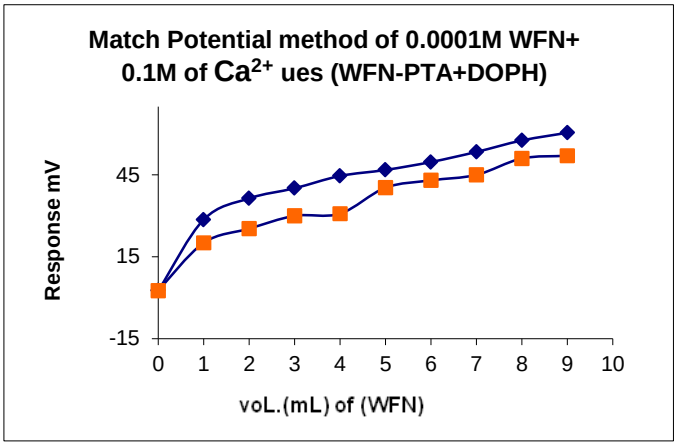


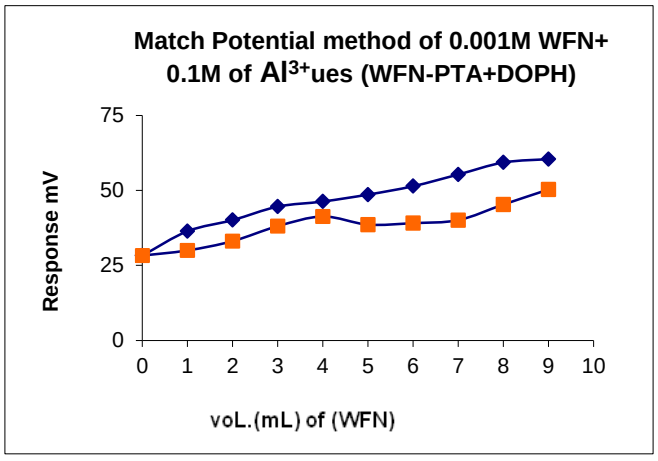
Figure (3.25) Selectivity of electrode (WFN-PTA) for (10^{-3} and 10^{-4}) M based on AP, for cation and amino acid interfering by match potential method, ■ Solutions of interfering , ♦ WFN solutions.

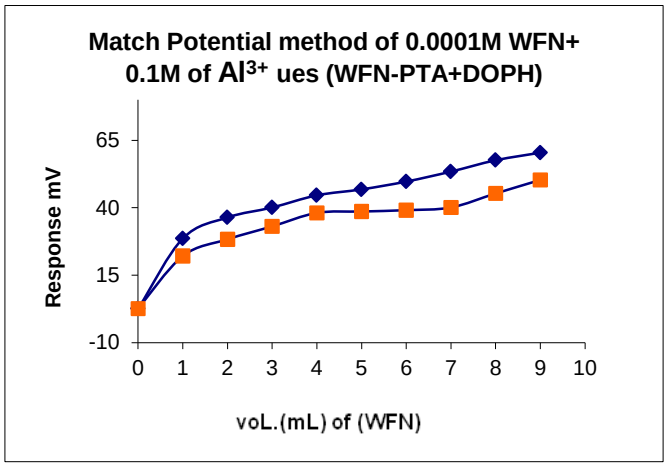

Match Potential method of 0.001M WFN+ 0.1M of K1+ues (WFN-PTA+DOPH)
Response mV
70
50
30
10
0 1 2 3 4 5 6 7 8 9 10
voL.(mL) of (WFN)


Match Potential method of 0.0001M WF+ 0.1M of K1+ ues (WFN-PTA+DOPH)
Response mV
65
40
15
-10
0 1 2 3 4 5 6 7 8 9 10
voL.(mL) of (WFN)


Match Potential method of 0.001M WFN+ 0.1M of Ca2+ues (WFN-PTA+DOPH)
Response mV
65
50
35
20
0 1 2 3 4 5 6 7 8 9 10
voL.(mL) of (WFN)


Match Potential method of 0.0001M WFN+ 0.1M of Ca2+ ues (WFN-PTA+DOPH)
Response mV
45
15
-15
0 1 2 3 4 5 6 7 8 9 10
voL.(mL) of (WFN)


Match Potential method of 0.001M WFN+ 0.1M of Al3+ues (WFN-PTA+DOPH)
Response mV
75
50
25
0
0 1 2 3 4 5 6 7 8 9 10
voL.(mL) of (WFN)


Match Potential method of 0.0001M WFN+ 0.1M of Al3+ ues (WFN-PTA+DOPH)
Response mV
65
40
15
-10
0 1 2 3 4 5 6 7 8 9 10
voL.(mL) of (WFN)

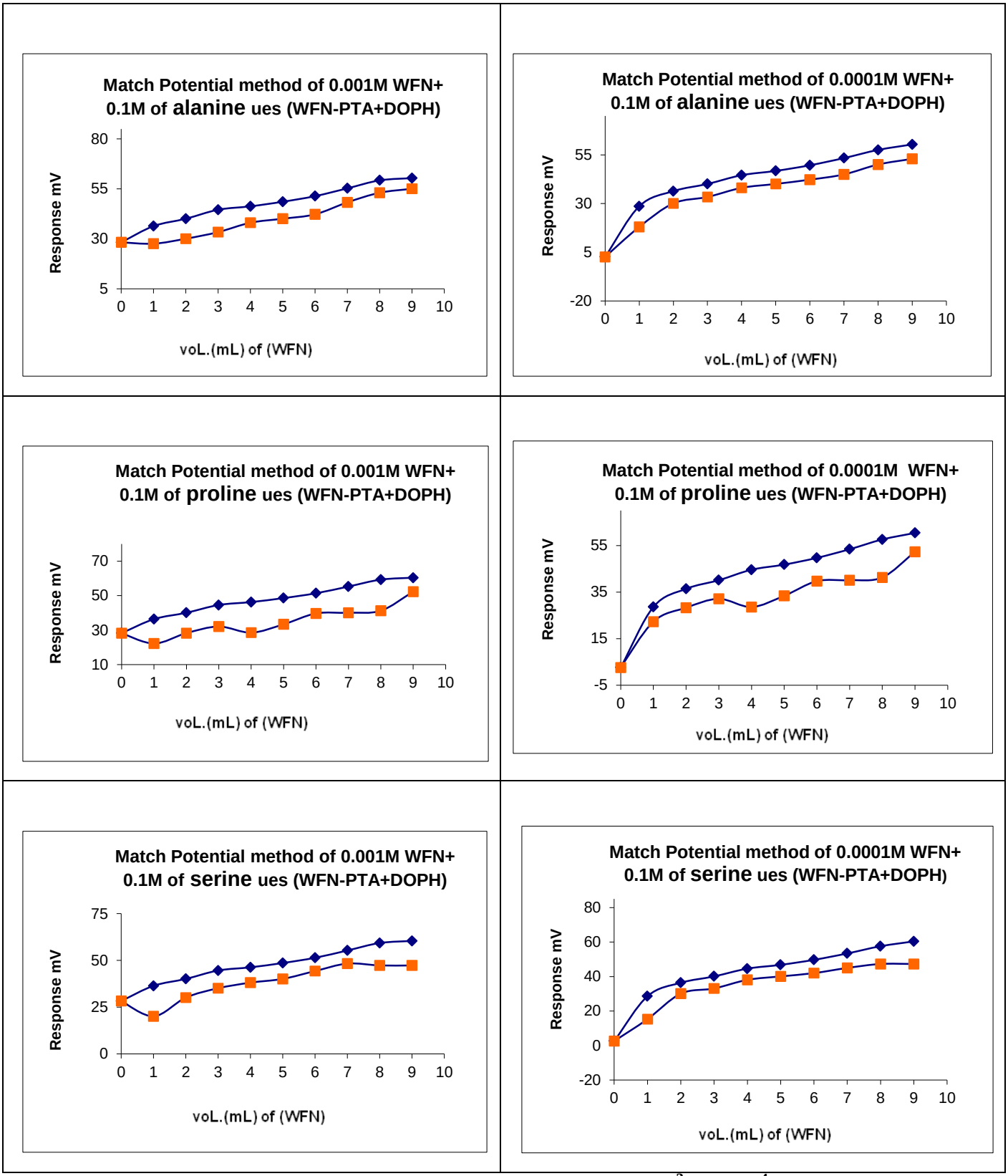


Figure (3.26) Selectivity of electrode (WFN-PTA) for (10^{-3} and 10^{-4}) M based on DOPH, for cation and amino acid interfering by match potential method, ■ Solutions of interfering , ♦ WFN solutions.

Table (3.16) Selectivity coefficients for the (WFN-MPA),(WFN-PTA) electrodes And (10^{-3}) M of Interfering-Ion determined by Match potential method (MPM) .

Plasticizers	Interfering-Ion (10^{-3}) M	K_{pot} (WFN- MPA)	K_{pot} (WFN- PT A)
OA	K^+	2.143×10^{-2}	1.264×10^{-1}
	Ca^{2+}	5.314×10^{-2}	2.355×10^{-2}
	AL^{3+}	3.233×10^{-2}	3.241×10^{-2}
	Alanine	4.711×10^{-2}	1.253×10^{-1}
	Proline	6.441×10^{-2}	3.452×10^{-2}
	Serine	2.374×10^{-2}	2.112×10^{-2}
TBP	K^+	3.720×10^{-2}	2.341×10^{-2}
	Ca^{2+}	1.210×10^{-2}	3.472×10^{-2}
	AL^{3+}	2.121×10^{-2}	1.427×10^{-2}
	Alanine	5.261×10^{-2}	7.235×10^{-2}
	Proline	1.267×10^{-2}	4.356×10^{-2}
	Serine	7.321×10^{-2}	5.243×10^{-2}
NB	K^+	4.210×10^{-1}	1.853×10^{-1}
	Ca^{2+}	1.536×10^{-2}	2.578×10^{-2}
	AL^{3+}	2.360×10^{-2}	3.659×10^{-2}
	Alanine	5.261×10^{-1}	2.357×10^{-2}
	Proline	1.267×10^{-2}	2.369×10^{-2}
	Serine	1.431×10^{-2}	2.247×10^{-1}
AP	K^+	6.143×10^{-1}	2.357×10^{-2}
	Ca^{2+}	8.318×10^{-2}	5.247×10^{-2}
	AL^{3+}	9.222×10^{-3}	5.369×10^{-1}
	Alanine	5.950×10^{-1}	1.247×10^{-2}
	Proline	8.870×10^{-2}	4.365×10^{-2}

	Serine	9.220×10^{-1}	7.359×10^{-2}
DOPH	**K^+**	1.369×10^{-1}	1.258×10^{-1}
	Ca^{2+}	1.132×10^{-2}	2.369×10^{-2}
	AL^{3+}	5.525×10^{-2}	3.458×10^{-2}
	Alanine	2.123×10^{-2}	2.365×10^{-2}
	Proline	3.811×10^{-2}	4.265×10^{-2}
	Serine	2.511×10^{-1}	3.264×10^{-1}

Table (3.17) Selectivity coefficients for the (WFN-MPA),(WFN-PTA) electrodes And (10^{-4}) M of Interfering-Ion determined by Match potential method (MPM) .

Plasticizers	**Interfering-Ion (10^{-4}) M**	**K_{pot} (WFN- MPA)**	**K_{pot} (WFN- PTA)**
OA	**K^+**	3.113×10^{-1}	1.583×10^{-2}
	Ca^{2+}	2.314×10^{-1}	3.258×10^{-2}
	AL^{3+}	3.222×10^{-2}	2.357×10^{-2}
	Alanine	6.721×10^{-2}	4.369×10^{-2}
	Proline	2.319×10^{-2}	1.247×10^{-2}
	Serine	4.421×10^{-1}	3.698×10^{-2}
TPB	**K^+**	1.321×10^{-2}	2.471×10^{-2}
	Ca^{2+}	2.710×10^{-2}	1.211×10^{-2}
	AL^{3+}	4.213×10^{-2}	3.614×10^{-2}
	Alanine	2.330×10^{-2}	4.141×10^{-2}
	Proline	3.271×10^{-2}	1.364×10^{-2}
	Serine	6.261×10^{-2}	2.4713×10^{-1}
NB	**K^+**	1.015×10^{-2}	5.3471×10^{-2}
	Ca^{2+}	2.116×10^{-2}	4.378×10^{-2}
	AL^{3+}	2.631×10^{-2}	1.247×10^{-2}

NB	**Alanine**	4.261×10^{-1}	7.258×10^{-1}
	Proline	2.247×10^{-2}	3.564×10^{-2}
	Serine	3.231×10^{-1}	3.258×10^{-2}
AP	$\mathbf{K^{+}}$	5.040×10^{-1}	1.247×10^{-2}
	$\mathbf{Ca^{2+}}$	6.424×10^{-2}	1.254×10^{-2}
	$\mathbf{AL^{3+}}$	8.102×10^{-2}	4.369×10^{-1}
	Alanine	4.544×10^{-2}	4.258×10^{-2}
	Proline	6.551×10^{-1}	7.254×10^{-2}
	Serine	5.229×10^{-2}	4.333×10^{-1}
DOPH	$\mathbf{K^{+}}$	4.232×10^{-2}	1.474×10^{-2}
	$\mathbf{Ca^{2+}}$	1.125×10^{-2}	2.111×10^{-2}
	$\mathbf{AL^{3+}}$	3.313×10^{-2}	3.547×10^{-1}
	Alanine	3.111×10^{-1}	4.364×10^{-2}
	Proline	3.512×10^{-1}	1.247×10^{-2}
	Serine	2.635×10^{-2}	2.121×10^{-1}

3.7. Standard analysis:

The concentrations of solutions of warfarin sodium were determined using all the electrodes. Three potentiometric techniques were used for the determination of warfarin sodium namely direct, incremental (standard addition (SAM) and multiple standard addition (MSA)) and titration methods. The relative error RE% and relative standard deviation RSD% were calculate for each method.

3.7.1. Direct potentiometric method:

This is the simplest and most widely used method for obtaining quantitative result by using ion-selective electrode. A calibration curve was constructed and the concentration of the unknown was calculated by

linear equation of the calibration curve，the results are listed in table (3.40),(3.41)for different composition (WFN-MPA),(WFN-PTA) electrodes, respectively.

3.7.2. Incremental Methods:

In these methods, the concentration of standard solution of warfarin sodium used for measurement was ≈100 times higher than the concentration of sample that was used to decrease the dilution effect. It is carried out by a procedure with 0.1mL increment of 10^{-1} M warfarin sodium as standard and was added to 10 mL of sample as unknown. The calculation can be used as following;

1-Standard Addition Method (SAM) .

2-Multiple Standard Addition (MSA)

3.7.2.1.Calculation of Standard Addition Method (SAM):

In this method concentrations of (10^{-3} and 10^{-4}) M for the ten warfarin sodium electrodes using equation (1-10) are listed in Tables (3.18) to (3.27) for (WFN-MPA) and (3.28) to (3.37) for (WFN-PTA) The RSD% and RE % were calculate from the results obtained for each method are given in Tables(3.40),(3.41) for (WFN-MPA), (WFN-PTA) respectively .

Table (3.18): Potential of 10^{-3}M warfarin sodium against the volume of standard warfarin Sodium and the calculation of five additions using MSA and SAM. For WFN-MPA+ OA electrode

V_S mL added	E/mV	*Antilog*E/S	Δ E	*Antilog*ΔE/S	(V_U/V_S)	C_U M
0	386.2	1.710×10^{12}	---	---	---	
0.1	395.6	3.395×10^{12}	9.4	1.984	100	1.006×10^{-3}
0.2	401.1	5.071×10^{12}	14.9	2.964	50	1.008×10^{-3}
0.3	405.2	6.838×10^{12}	19.0	3.997	33.33	0.991×10^{-3}
0.4	408.4	8.636×10^{12}	22.2	5.048	25	0.978×10^{-3}
0.5	410.7	10.213×10^{12}	24.5	5.971	20	0.995×10^{-3}

Table (3.19): Potential of 10^{-4}M warfarin sodium against the volume of standard warfarin Sodium and the calculation of five additions using MSA and SAM. For WFN-MPA+ OA electrode

V_S mL added	E/mV	*Antilog*E/S	Δ E	*Antilog*ΔE/S	(V_U/V_S)	C_U M
0	355.1	0.177×10^{12}	---	---	---	
0.1	387.8	1.922×10^{12}	32.7	10.859	100	1.013×10^{-4}
0.2	397.2	3.815×10^{12}	42.1	21.554	50	0.972×10^{-4}
0.3	402.7	5.698×10^{12}	47.6	32.192	33.33	0.960×10^{-4}
0.4	405.9	7.196×10^{12}	50.8	40.655	25	1.007×10^{-4}
0.5	409.3	9.222×10^{12}	54.2	52.097	20	0.977×10^{-4}

Table (3.20): Potential of 10^{-3}M warfarin sodium against the volume of standard warfarin Sodium and the calculation of five additions using MSA and SAM. For WFN-MPA+ TBP electrode

V_S mL added	E/mV	*Antilog*E/S	Δ E	*Antilog*ΔE/S	(V_U/V_S)	C_U M
0	103.1	0.470×10^{4}	---	---	---	
0.1	111.7	0.953×10^{4}	8.6	2.024	100	0.967×10^{-3}
0.2	116.1	1.368×10^{4}	13	2.904	50	1.039×10^{-3}
0.3	119.6	1.822×10^{4}	16.5	3.870	33.33	1.034×10^{-3}
0.4	122.7	2.350×10^{4}	19.6	4.991	25	0.992×10^{-3}
0.5	124.7	2.769×10^{4}	21.6	5.881	20	1.013×10^{-3}

Table (3.21): Potential of 10^{-4}M warfarin sodium against the volume of standard warfarin Sodium and the calculation of five additions using MSA and SAM. For WFN-MPA+ TBP electrode

V_S mL added	E/mV	*Antilog*E/S	Δ E	*Antilog*ΔE/S	(V_U/V_S)	C_U M
0	74.8	0.046×10^4	---	---	---	
0.1	105.2	0.559×10^4	30.4	12.007	100	0.907×10^{-4}
0.2	112.0	0.977×10^4	37.2	21.147	50	0.990×10^{-4}
0.3	116.9	1.460×10^4	42.1	31.609	33.33	0.979×10^{-4}
0.4	120.6	1.978×10^4	45.8	42.818	25	0.956×10^{-4}
0.5	123.2	2.449×10^4	48.4	52.998	20	0.960×10^{-4}

Table (3.22): Potential of 10^{-3}M warfarin sodium against the volume of standard warfarin Sodium and the calculation of five additions using MSA and SAM. For WFN-MPA+ NB electrode

V_S mL added	E/mV	*Antilog*E/S	Δ E	*Antilog*ΔE/S	(V_U/V_S)	C_U M
0	179.8	1.495×10^7	---	---	---	
0.1	186.6	2.793×10^7	6.8	1.867	100	1.110×10^{-3}
0.2	191.7	4.463×10^7	11.9	2.984	50	0.998×10^{-3}
0.3	195.0	6.044×10^7	15.2	4.041	33.33	0.977×10^{-3}
0.4	197.4	7.535×10^7	17.6	5.038	25	0.980×10^{-3}
0.5	199.1	8.809×10^7	19.3	5.890	20	1.012×10^{-3}

Table (3.23): Potential of 10^{-4}M warfarin sodium against the volume of standard warfarin Sodium and the calculation of five additions using MSA and SAM. For WFN-MPA+ NB electrode

V_S mL added	E/mV	*Antilog*E/S	Δ E	*Antilog*ΔE/S	(V_U/V_S)	C_U M
0	155.5	0.160×10^{7}	---	---	---	
0.1	180.3	1.565×10^{7}	24.8	9.763	100	1.130×10^{-4}
0.2	187.8	3.118×10^{7}	32.3	19.449	50	1.082×10^{-4}
0.3	192.7	4.892×10^{7}	37.2	30.509	33.33	1.015×10^{-4}
0.4	195.1	6.099×10^{7}	39.6	38.037	25	1.078×10^{-4}
0.5	197.5	7.604×10^{7}	42.0	47.421	20	1.075×10^{-4}

Table (3.24): Potential of 10^{-3}M warfarin sodium against the volume of standard warfarin Sodium and the calculation of five additions using MSA and SAM. For WFN-MPA+ AP electrode

V_S mL added	E/mV	*Antilog*E/S	Δ E	*Antilog*ΔE/S	(V_U/V_S)	C_U M
0	22.1	1.092×10^{1}	---	---	---	
0.1	28.4	2.160×10^{1}	6.3	1.977	100	1.013×10^{-3}
0.2	32.3	3.295×10^{1}	10.2	3.015	50	0.982×10^{-3}
0.3	34.8	4.318×10^{1}	12.7	3.951	33.33	1.006×10^{-3}
0.4	36.7	5.304×10^{1}	14.6	4.853	25	1.027×10^{-3}
0.5	38.6	6.514×10^{1}	16.5	5.961	20	0.997×10^{-3}

Table (3.25): Potential of 10^{-4}M warfarin sodium against the volume of standard warfarin Sodium and the calculation of five additions using MSA and SAM. For WFN-MPA+ AP electrode

V_S mL added	E/mV	*Antilog*E/S	Δ E	*Antilog*ΔE/S	(V_U/V_S)	C_U M
0	2.0	0.124×10^{1}	---	---	---	
0.1	25.0	1.495×10^{1}	23.0	12.045	100	0.904×10^{-4}
0.2	30.5	2.711×10^{1}	28.5	21.841	50	0.958×10^{-4}
0.3	33.9	3.917×10^{1}	31.9	31.554	33.33	0.981×10^{-4}
0.4	36.8	5.361×10^{1}	34.8	43.185	25	0.950×10^{-4}
0.5	38.8	6.657×10^{1}	36.8	53.619	20	0.951×10^{-4}

Table (3.26): Potential of 10^{-3}M warfarin sodium against the volume of standard warfarin Sodium and the calculation of five additions using MSA and SAM. For WFN-MPA+ DOPH electrode

V_S mL added	E/mV	*Antilog*E/S	Δ E	*Antilog*ΔE/S	(V_U/V_S)	C_U M
0	209.3	0.853×10^{8}	---	---	---	
0.1	217.5	1.744×10^{8}	8.2	2.045	100	0.950×10^{-3}
0.2	221.8	2.539×10^{8}	12.5	2.976	50	1.002×10^{-3}
0.3	225.0	3.357×10^{8}	15.7	3.934	33.33	1.012×10^{-3}
0.4	227.7	4.248×10^{8}	18.4	4.980	25	0.995×10^{-3}
0.5	230.0	5.193×10^{8}	20.7	6.086	20	0.973×10^{-3}

Table (3.27): Potential of 10^{-4}M warfarin sodium against the volume of standard warfarin Sodium and the calculation of five additions using MSA and SAM. For WFN-MPA+ DOPH electrode

V_S mL added	E/mV	*Antilog*E/S	Δ E	*Antilog*ΔE/S	(V_U/V_S)	C_U M
0	183.2	0.087×10^{8}	---	---	---	
0.1	211.1	0.998×10^{8}	27.9	11.408	100	0.959×10^{-4}
0.2	218.0	1.822×10^{8}	34.8	20.829	50	1.007×10^{-4}
0.3	222.4	2.675×10^{8}	39.2	30.578	33.33	1.013×10^{-4}
0.4	225.9	3.631×10^{8}	42.7	41.498	25	0.986×10^{-4}
0.5	228.3	4.477×10^{8}	45.1	51.165	20	0.995×10^{-4}

Table (3.28): Potential of 10^{-3}M warfarin sodium against the volume of standard warfarin Sodium and the calculation of five additions using MSA and SAM. For WFN-PTA+ OA electrode

V_S mL added	E/mV	*Antilog*E/S	Δ E	*Antilog*ΔE/S	(V_U/V_S)	C_U M
0	66.1	1.704×10^{2}	--	--	--	--
0.1	75.3	3.484×10^{2}	9.2	2.044	100	0.948×10^{-3}
0.2	80.0	5.022×10^{2}	13.9	2.946	50	1.017×10^{-3}
0.3	83.5	6.592×10^{2}	17.4	3.867	33.33	1.035×10^{-3}
0.4	86.6	8.388×10^{2}	20.5	4.921	25.	1.009×10^{-3}
0.5	89.4	10.428×10^{2}	23.3	6.118	20	0.967×10^{-3}

Table (3.29): Potential of 10^{-4}M warfarin sodium against the volume of standard warfarin Sodium and the calculation of five additions using MSA and SAM. For WFN-PTA+ OA electrode

V_S mL added	E/mV	*Antilog*E/S	Δ E	*Antilog*ΔE/S	(V_U/V_S)	C_U M
0	35.8	0.161×10^{2}	--	--	--	--
0.1	66.5	1.758×10^{2}	30.7	10.875	100	1.011×10^{-4}
0.2	74.2	3.199×10^{2}	38.4	19.788	50	1.063×10^{-4}
0.3	79.5	4.830×10^{2}	43.7	29.878	33.33	1.037×10^{-4}
0.4	83.1	6.390×10^{2}	47.3	39.527	25	1.037×10^{-4}
0.5	85.9	7.944×10^{2}	50.1	49.138	20	1.037×10^{-4}

Table (3.30): Potential of 10^{-3}M warfarin sodium against the volume of standard warfarin Sodium and the calculation of five additions using MSA and SAM. For WFN-PTA+ TBP electrode

V_S mL added	E/mV	*Antilog*E/S	Δ E	*Antilog*ΔE/S	(V_U/V_S)	C_U M
0	41.1	0.311×10^{2}	--	--	--	--
0.1	49.5	0.628×10^{2}	8.4	2.018	100	0.972×10^{-3}
0.2	54.2	0.930×10^{2}	13.1	2.991	50	0.994×10^{-3}
0.3	57.8	1.257×10^{2}	16.7	4.042	33.33	0.976×10^{-3}
0.4	60.1	1.524×10^{2}	19.0	4.899	25	1.015×10^{-3}
0.5	62.8	1.910×10^{2}	21.7	6.140	20	0.963×10^{-3}

Table (3.31): Potential of 10^{-4}M warfarin sodium against the volume of standard warfarin Sodium and the calculation of five additions using MSA and SAM. For WFN-PTA+ TBP electrode

V_S mL added	E/mV	*Antilog*E/S	Δ E	*Antilog*ΔE/S	(V_U/V_S)	C_U M
0	12.9	0.294×10^{1}	--	--	--	--
0.1	41.8	3.298×10^{1}	28.9	11.214	100	0.978×10^{-4}
0.2	48.8	5.923×10^{1}	35.9	20.138	50	1.043×10^{-4}
0.3	55.1	10.033×10^{1}	42.2	34.109	33.33	0.905×10^{-4}
0.4	57.4	12.161×10^{1}	44.5	41.344	25	0.990×10^{-4}
0.5	60.1	15.243×10^{1}	47.2	51.819	20	0.982×10^{-4}

Table (3.32): Potential of 10^{-3}M warfarin sodium against the volume of standard warfarin Sodium and the calculation of five additions using MSA and SAM. For WFN-PTA+ NB electrode

V_S mL added	E/mV	*Antilog*E/S	Δ E	*Antilog*ΔE/S	(V_U/V_S)	C_U M
0	-57.9	0.454×10^{-2}	--	--	--	--
0.1	-50.4	0.914×10^{-2}	7.5	2.010	100	0.980×10^{-3}
0.2	-45.9	1.390×10^{-2}	12.0	3.057	50	0.962×10^{-3}
0.3	-43.1	1.788×10^{-2}	14.7	3.932	33.33	1.012×10^{-3}
0.4	-40.8	2.236×10^{-2}	17.1	4.917	25	1.010×10^{-3}
0.5	-38.6	2.744×10^{-2}	19.3	6.035	20	0.983×10^{-3}

Table (3.33): Potential of 10^{-4}M warfarin sodium against the volume of standard warfarin Sodium and the calculation of five additions using MSA and SAM. For WFN-PTA+ NB electrode

V_S mL added	E/mV	*Antilog*E/S	Δ E	*Antilog*ΔE/S	(V_U/V_S)	C_U M
0	-83.1	0.043×10^{-2}	--	--	--	--
0.1	-57.6	0.467×10^{-2}	25.5	10.753	100	1.024×10^{-4}
0.2	-50.3	0.923×10^{-2}	32.8	21.225	50	0.987×10^{-4}
0.3	-46.4	1.327×10^{-2}	36.7	30.523	33.33	1.015×10^{-4}
0.4	-43.2	1.788×10^{-2}	39.9	41.122	25	0.995×10^{-4}
0.5	-41.0	2.194×10^{-2}	42.1	50.474	20	1.009×10^{-4}

Table (3.34): Potential of 10^{-3}M warfarin sodium against the volume of standard warfarin Sodium and the calculation of five additions using MSA and SAM. For WFN-PTA+ AP electrode

V_S mL added	E/mV	*Antilog*E/S	Δ E	*Antilog*ΔE/S	(V_U/V_S)	C_U M
0	-97.9	1.302×10^{-5}	--	--	--	--
0.1	-91.8	2.625×10^{-5}	6.1	2.015	100	0.975×10^{-3}
0.2	-88.2	3.970×10^{-5}	9.7	3.048	50	0.967×10^{-3}
0.3	-85.7	5.291×10^{-5}	12.2	4.062	33.33	0.970×10^{-3}
0.4	-83.9	6.507×10^{-5}	14.0	4.995	25	0.991×10^{-3}
0.5	-82.1	8.001×10^{-5}	15.8	6.143	20	0.962×10^{-3}

Table (3.35): Potential of 10^{-4}M warfarin sodium against the volume of standard warfarin Sodium and the calculation of five additions using MSA and SAM. For WFN-PTA+ AP electrode

V_S mL added	E/mV	*Antilog*E/S	Δ E	*Antilog*ΔE/S	(V_U/V_S)	C_U M
0	-117.9	0.130×10^{-5}	--	--	--	--
0.1	-96.9	1.461×10^{-5}	21.0	11.166	100	0.982×10^{-4}
0.2	-91.1	2.845×10^{-5}	26.9	21.743	50	0.963×10^{-4}
0.3	-88.9	3.663×10^{-5}	29.0	27.996	33.33	1.110×10^{-4}
0.4	-86.0	5.111×10^{-5}	31.9	39.067	25	1.049×10^{-4}
0.5	-83.6	6.735×10^{-5}	34.3	51.472	20	0.989×10^{-4}

Table (3.36): Potential of 10^{-3}M warfarin sodium against the volume of standard warfarin Sodium and the calculation of five additions using MSA and SAM. For WFN-PTA+ DOPH electrode

V_S mL added	E/mV	*Antilog*E/S	Δ E	*Antilog*ΔE/S	(V_U/V_S)	C_U M
0	26.3	1.026×10^{1}	--	--	--	--
0.1	34.1	2.048×10^{1}	7.8	1.995	100	0.995×10^{-3}
0.2	38.6	3.052×10^{1}	12.3	2.972	50	1.004×10^{-3}
0.3	42.2	4.198×10^{1}	15.9	4.088	33.33	0.962×10^{-3}
0.4	44.0	4.923×10^{1}	17.7	4.794	25	1.043×10^{-3}
0.5	46.6	6.198×10^{1}	20.3	6.036	20	0.983×10^{-3}

Table (3.37): Potential of 10^{-4}M warfarin sodium against the volume of standard warfarin Sodium and the calculation of five additions using MSA and SAM. For WFN-PTA+ DOPH electrode

V_S mL added	E/mV	*Antilog*E/S	Δ E	*Antilog*ΔE/S	(V_U/V_S)	C_U M
0	1.1	0.110×10^{1}	--	--	--	--
0.1	28.2	1.215×10^{1}	27.1	11.023	100	0.996×10^{-4}
0.2	35.7	2.360×10^{1}	34.6	21.417	50	0.978×10^{-4}
0.3	39.5	3.305×10^{1}	38.4	29.986	33.33	1.034×10^{-4}
0.4	43.1	4.546×10^{1}	42.0	41.246	25	0.992×10^{-4}
0.5	45.5	5.623×10^{1}	44.4	51.014	20	0.998×10^{-4}

3.7.2.2. Calculation of Multiple Standard Method (MSM):

In this method two solutions of warfarin sodium at concentrations of 10^{-3}M and 10^{-4}M were used to plot antilog E/S versus volume of standard warfarin sodium . The results of the concentrations of warfarin sodium calculated using the electrodes of (WFN-MPA),(WFN-PTA) based on OA, TBP , NB, AP and DOPH and these are shown in Figurs (3.27) to (3.36) for (WFN-MPA)and(3.37) to (3.46) for (WFN-PTA). From the equations (1-11) of calibration curves, the volume (V) mL at intercept with X axis for each curve was calculated. The linear equations of the calibration curves for MSM, their correlation coefficients, (V) and (C_U) were listed in Table (3.38),(3.39) for (WFN-MPA),(WFN-PTA) respectively .

WFN- MPA+ OA Slope = 31.57 Reading	
V(ml)	Antilog(E/S)
0	1.710×10^{12}
0.1	3.395×10^{12}
0.2	5.071×10^{12}
0.3	6.838×10^{12}
0.4	8.636×10^{12}
0.5	10.213×10^{12}

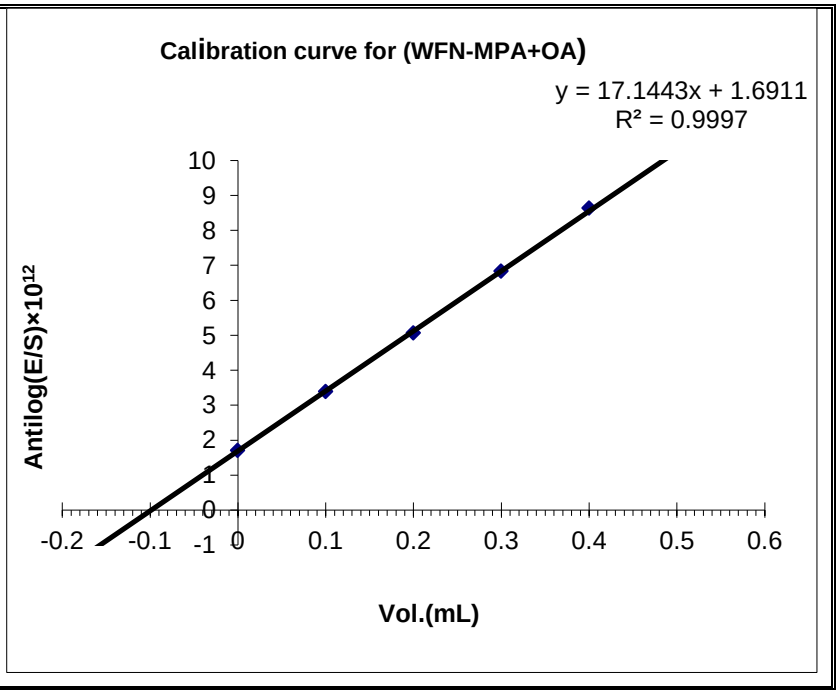


Figure (3.27): Antilog (E/S) versus the volume of the added standard for the determination of warfarin solution (10^{-3}M) by MSM using WFN-MPA+OA electrode

WFN- MPA+ OA Slope = 31.57 Reading	
V(ml)	Antilog(E/S)
0	0.177×10^{12}
0.1	1.922×10^{12}
0.2	3.815×10^{12}
0.3	5.698×10^{12}
0.4	7.196×10^{12}
0.5	9.222×10^{12}

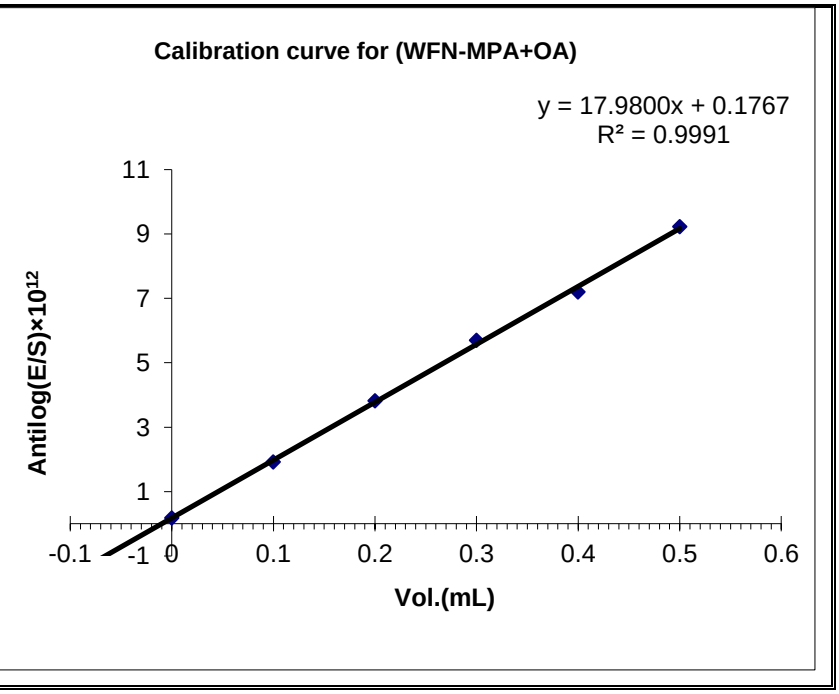


Figure (3.28): Antilog (E/S) versus the volume of the added standard for the determination of warfarin solution (10^{-4}M) by MSM using WFN-MPA+OA electrode

WFN- MPA+ TBP Slope = 28.07 Reading	
V(ml)	Antilog(E/S)
0	0.470×10^4
0.1	0.953×10^4
0.2	1.368×10^4
0.3	1.822×10^4
0.4	2.350×10^4
0.5	2.769×10^4

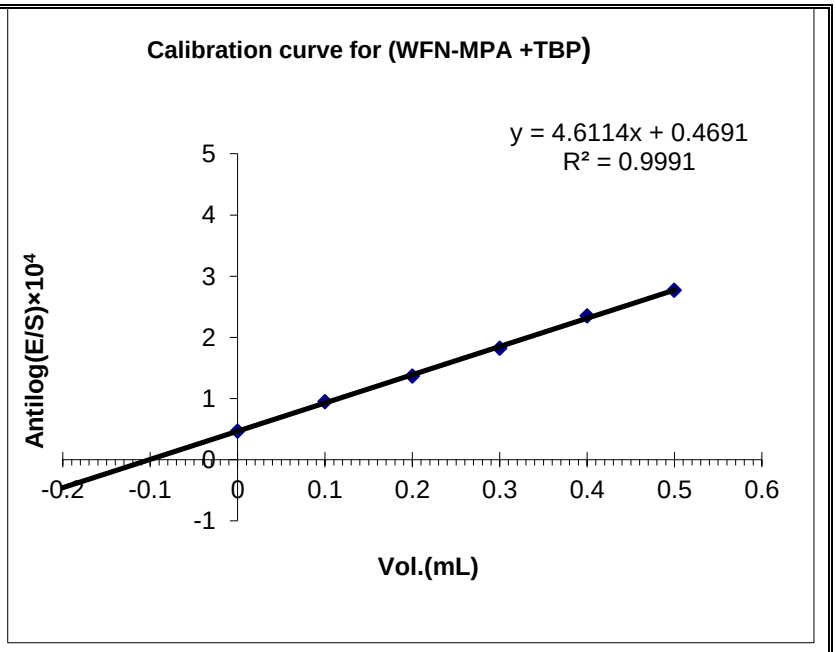


Figure (3.29): Antilog (E/S) versus the volume of the added standard for the determination of warfarin solution (10^{-3}M) by MSM using WFN-MPA+TBP electrode

WFN- MPA+ TBP Slope = 28.07 Reading	
V(ml)	Antilog(E/S)
0	0.046×10^4
0.1	0.559×10^4
0.2	0.977×10^4
0.3	1.460×10^4
0.4	1.978×10^4
0.5	2.449×10^4

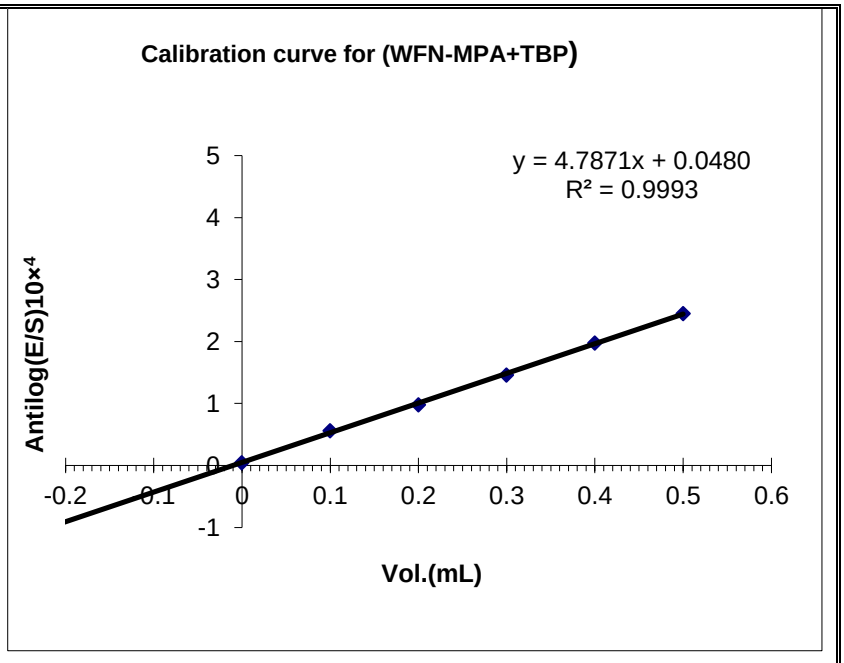


Figure (3.30): Antilog (E/S) versus the volume of the added standard for the determination of warfarin solution (10^{-4}M) by MSM using WFN-MPA+TBP electrode

WFN- MPA+ NB Slope = 25.06 Reading	
V(ml)	Antilog(E/S)
0	1.495×10^{7}
0.1	2.793×10^{7}
0.2	4.463×10^{7}
0.3	6.044×10^{7}
0.4	7.535×10^{7}
0.5	8.809×10^{7}

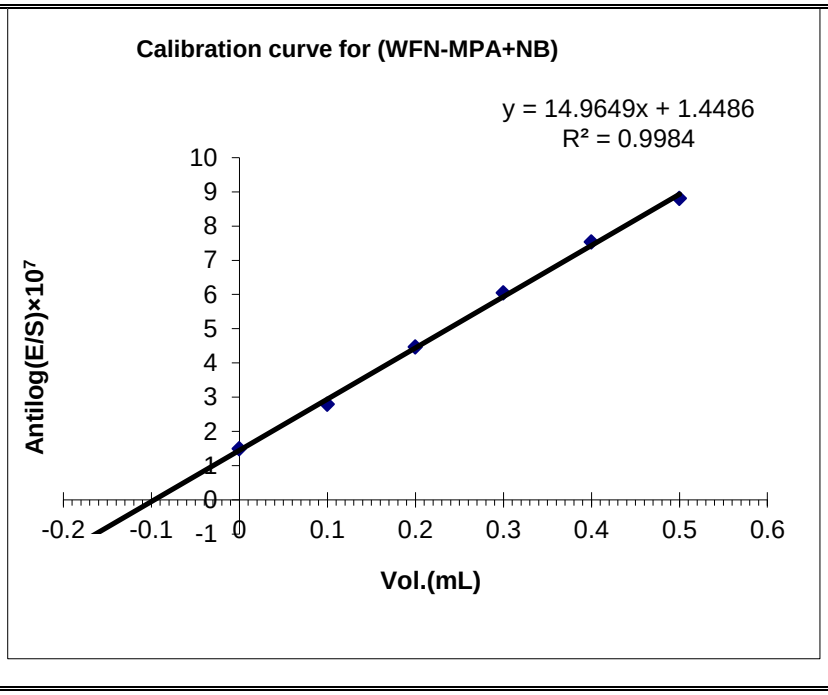


Figure (3.31): Antilog (E/S) versus the volume of the added standard for the determination of warfarin solution (10^{-3}M) by MSM using WFN-MPA+NB electrode

WFN- MPA+ NB Slope = 25.06 Reading	
V(ml)	Antilog(E/S)
0	0.160×10^{7}
0.1	1.565×10^{7}
0.2	3.118×10^{7}
0.3	4.892×10^{7}
0.4	6.099×10^{7}
0.5	7.604×10^{7}

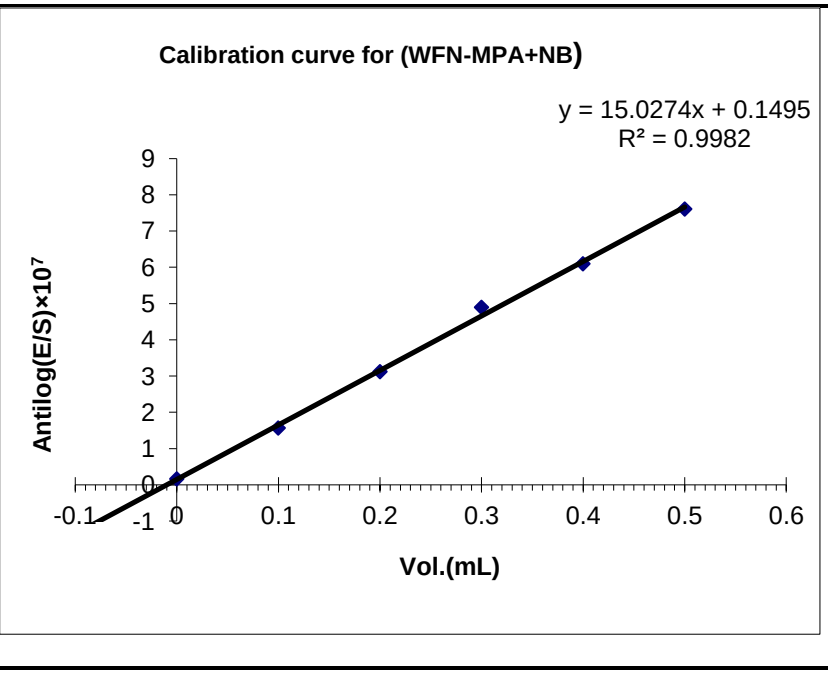


Figure (3.32): Antilog (E/S) versus the volume of the added standard for the determination of warfarin solution (10^{-4}M) by MSM using WFN-MPA+NB electrode

WFN- MPA+ AP Slope =21.28 Reading	
V(ml)	Antilog(E/S)
0	1.092×10^{1}
0.1	2.160×10^{1}
0.2	3.295×10^{1}
0.3	4.318×10^{1}
0.4	5.304×10^{1}
0.5	6.514×10^{1}

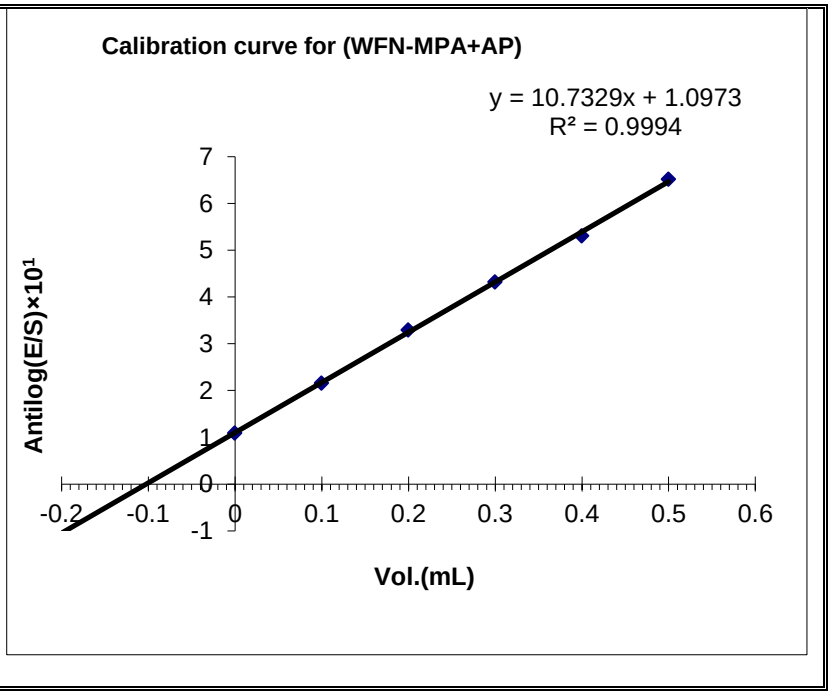


Figure (3.33): Antilog (E/S) versus the volume of the added standard for the determination of warfarin solution (10^{-3}M) by MSM using WFN-MPA+AP electrode

WFN- MPA+ AP Slope = 21.28 Reading	
V(ml)	Antilog(E/S)
0	0.124×10^{1}
0.1	1.495×10^{1}
0.2	2.711×10^{1}
0.3	3.917×10^{1}
0.4	5.361×10^{1}
0.5	6.657×10^{1}

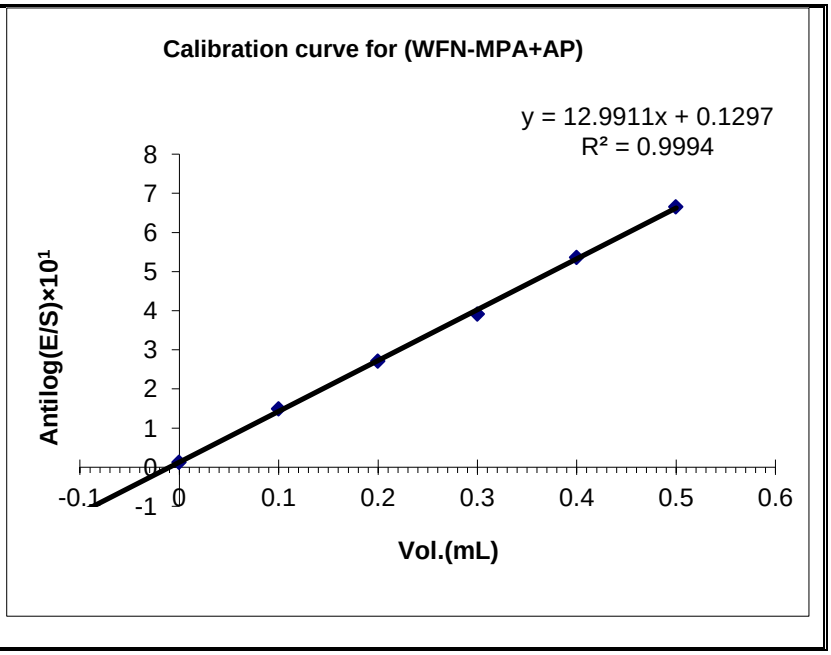


Figure (3.34): Antilog (E/S) versus the volume of the added standard for the determination of warfarin solution (10^{-4}M) by MSM using WFN-MPA+AP electrode

WFN- MPA+ DOPH Slope = 26.39 Reading	
V(ml)	Antilog(E/S)
0	0.853×10^{8}
0.1	1.744×10^{8}
0.2	2.539×10^{8}
0.3	3.357×10^{8}
0.4	4.248×10^{8}
0.5	5.193×10^{8}

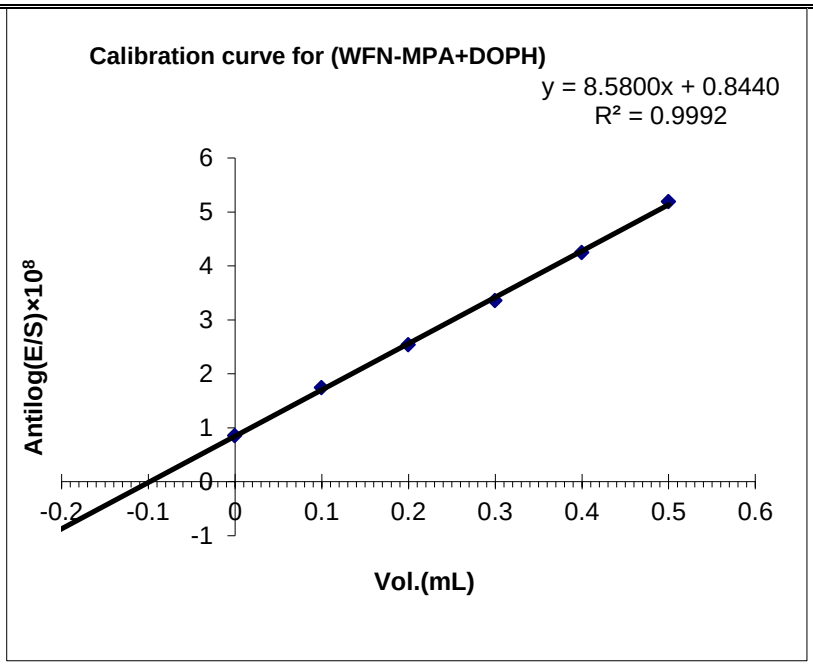


Figure (3.35): Antilog (E/S) versus the volume of the added standard for the determination of warfarin solution (10^{-3}M) by MSM using WFN-MPA+DOPH electrode

WFN- MPA+ DOPH Slope =26.39 Reading	
V(ml)	Antilog(E/S)
0	0.087×10^{8}
0.1	0.998×10^{8}
0.2	1.822×10^{8}
0.3	2.675×10^{8}
0.4	3.631×10^{8}
0.5	4.477×10^{8}

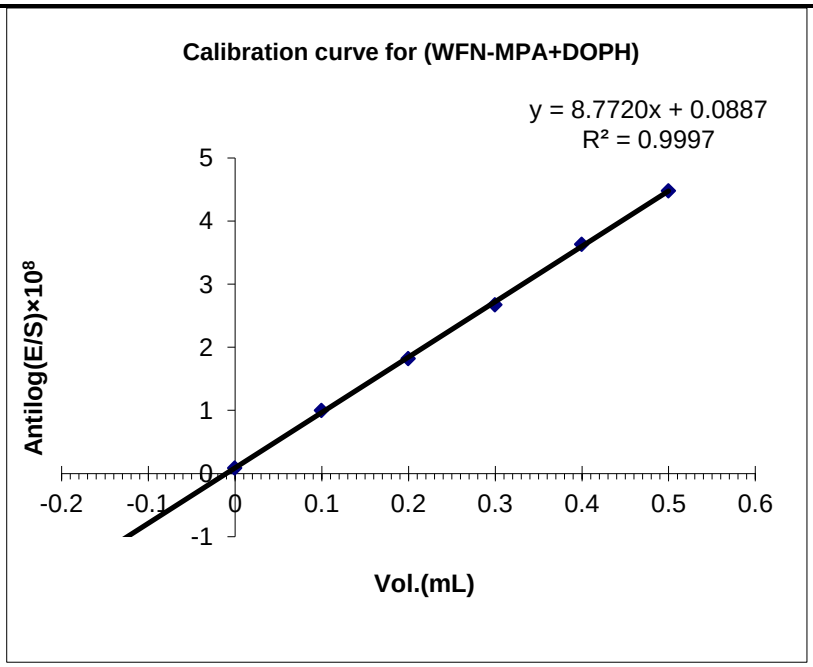
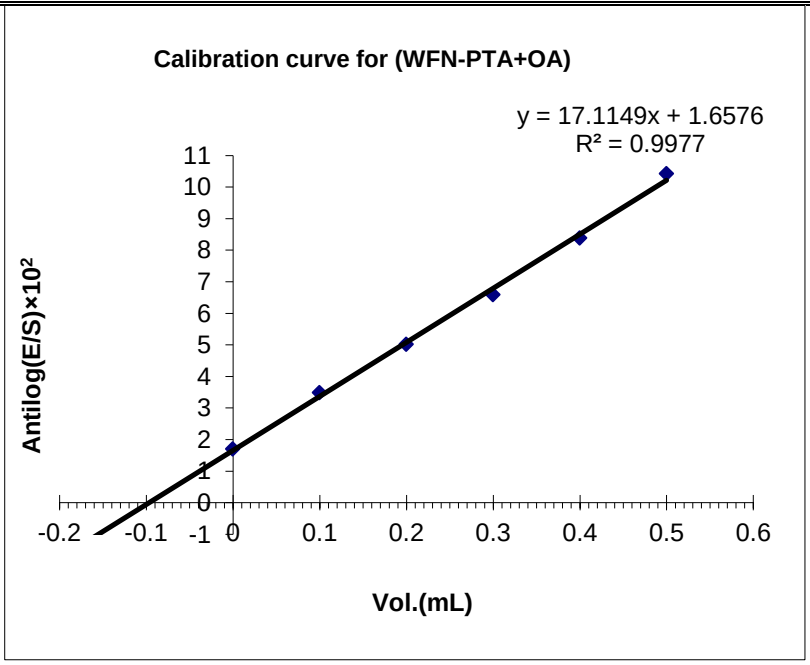


Figure (3.36): Antilog (E/S) versus the volume of the added standard for the determination of warfarin solution (10^{-4}M) by MSM using WFN-MPA+DOPH electrode

WFN- PTA+ OA Slope =29.62 Reading	
V(ml)	Antilog(E/S)
0	1.704×10^2
0.1	3.484×10^2
0.2	5.022×10^2
0.3	6.592×10^2
0.4	8.388×10^2
0.5	10.428×10^2



Figure(3.37): Antilog (E/S) versus the volume of the added standard for the determination of warfarin solution (10^{-3}M) by MSM using WFN-PTA+OA electrode

WFN- PTA+ OA Slope =29.62 Reading	
V(ml)	Antilog(E/S)
0	0.161×10^2
0.1	1.758×10^2
0.2	3.199×10^2
0.3	4.830×10^2
0.4	6.390×10^2
0.5	7.944×10^2

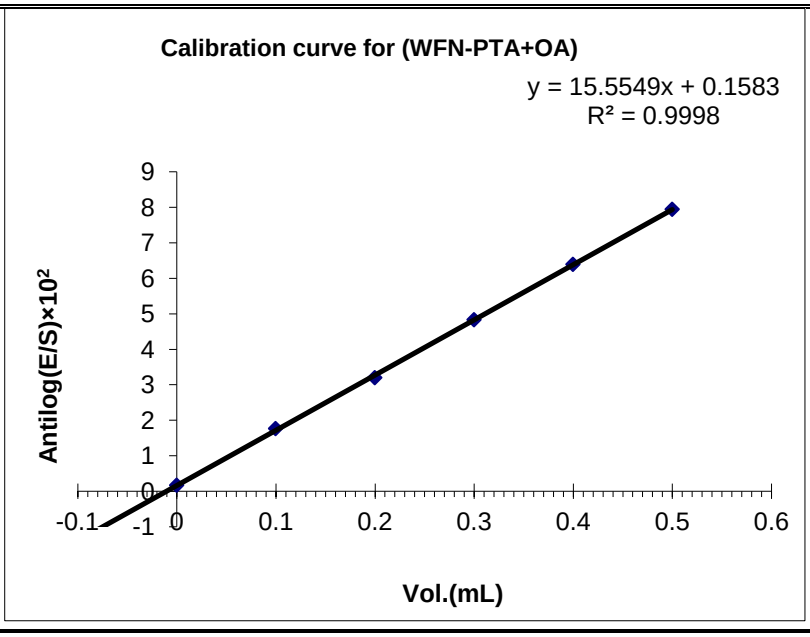


Figure (3.38): Antilog (E/S) versus the volume of the added standard for the determination of warfarin solution (10^{-4}M) by MSM using WFN-PTA+OA electrode

WFN- PTA+ TBP Slope =27.53 Reading	
V(ml)	Antilog(E/S)
0	0.311×10^{2}
0.1	0.628×10^{2}
0.2	0.930×10^{2}
0.3	1.257×10^{2}
0.4	1.524×10^{2}
0.5	1.910×10^{2}

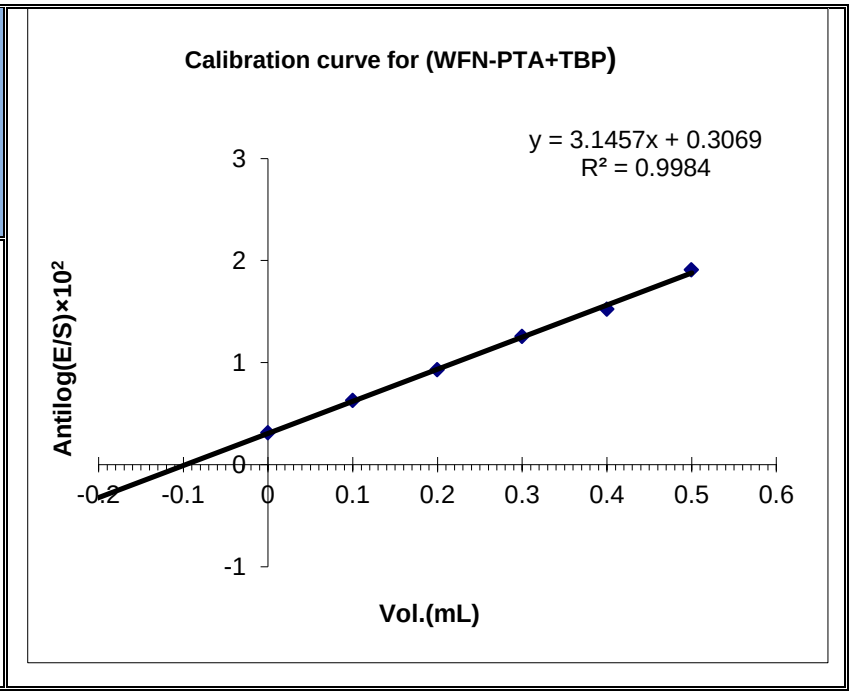


Figure (3.39): Antilog (E/S) versus the volume of the added standard for the determination of warfarin solution (10^{-3}M) by MSM using WFN-PTA+TBP electrode

WFN- PTA+ TBP Slope =27.53 Reading	
V(ml)	Antilog(E/S)
0	0.294×10^{1}
0.1	3.298×10^{1}
0.2	5.923×10^{1}
0.3	10.033×10^{1}
0.4	12.161×10^{1}
0.5	15.243×10^{1}

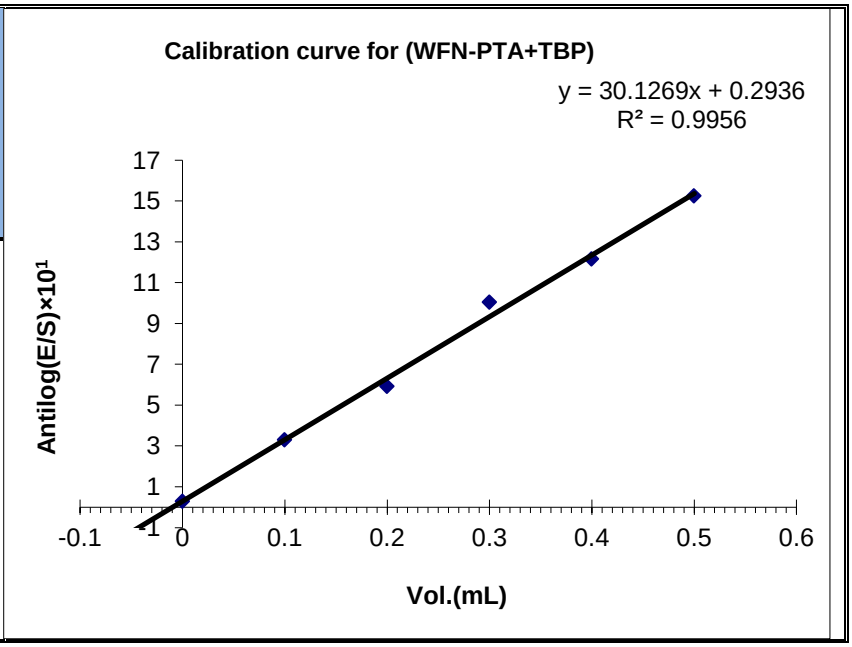


Figure (3.40): Antilog (E/S) versus the volume of the added standard for the determination of warfarin solution (10^{-4}M) by MSM using WFN-PTA+TBP electrode

WFN- PTA+ NB Slope =24.72 Reading	
V(ml)	Antilog(E/S)
0	0.454×10^{-2}
0.1	0.914×10^{-2}
0.2	1.390×10^{-2}
0.3	1.788×10^{-2}
0.4	2.236×10^{-2}
0.5	2.744×10^{-2}

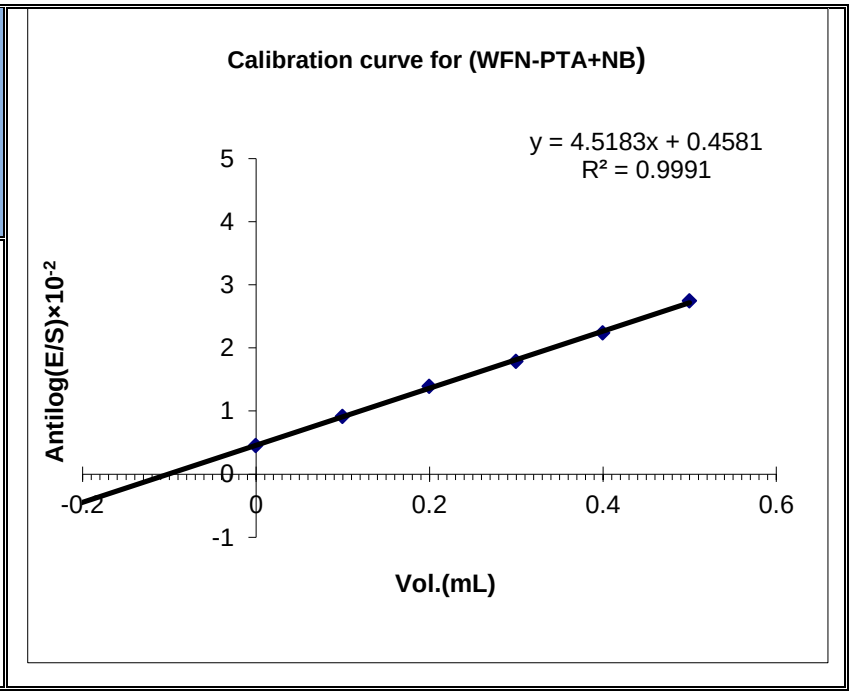


Figure (3.41): Antilog (E/S) versus the volume of the added standard for the determination of warfarin solution (10^{-3}M) by MSM using WFN-PTA+NB electrode

WFN- PTA+ NB Slope =24.72 Reading	
V(ml)	Antilog(E/S)
0	0.043×10^{-2}
0.1	0.467×10^{-2}
0.2	0.923×10^{-2}
0.3	1.327×10^{-2}
0.4	1.788×10^{-2}
0.5	2.194×10^{-2}

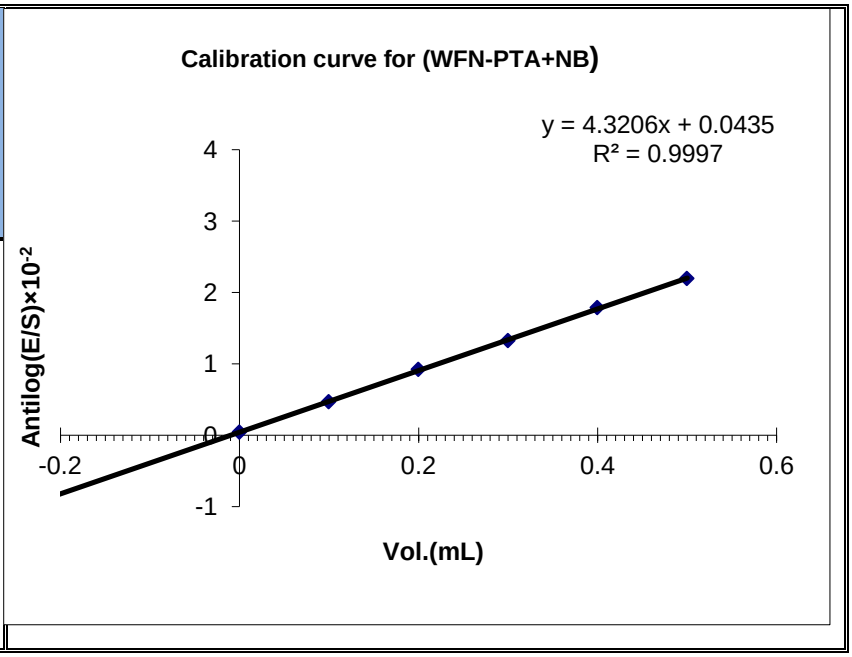


Figure (3.42): Antilog (E/S) versus the volume of the added standard for the determination of warfarin solution (10^{-4}M) by MSM using WFN-PTA+NB electrode

WFN- PTA+ AP Slope =20.04 Reading	
V(ml)	Antilog(E/S)
0	1.302×10^{-5}
0.1	2.625×10^{-5}
0.2	3.970×10^{-5}
0.3	5.291×10^{-5}
0.4	6.507×10^{-5}
0.5	8.001×10^{-5}

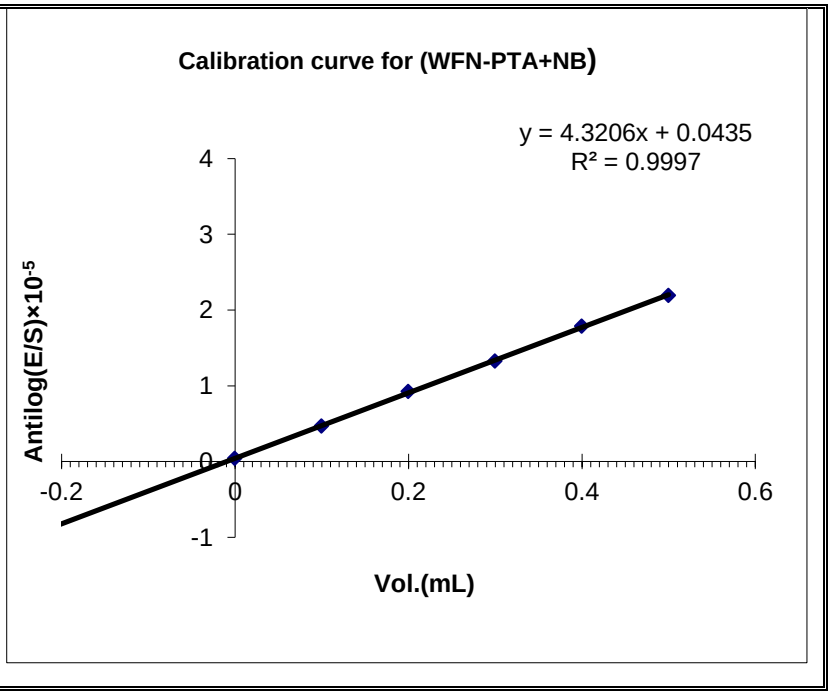


Figure (3.43): Antilog (E/S) versus the volume of the added standard for the determination of warfarin solution (10^{-3}M) by MSM using WFN-PTA+AP electrode

WFN- PTA+ AP Slope =20.04 Reading	
V(ml)	Antilog(E/S)
0	0.130×10^{-5}
0.1	1.461×10^{-5}
0.2	2.845×10^{-5}
0.3	3.663×10^{-5}
0.4	5.111×10^{-5}
0.5	6.735×10^{-5}

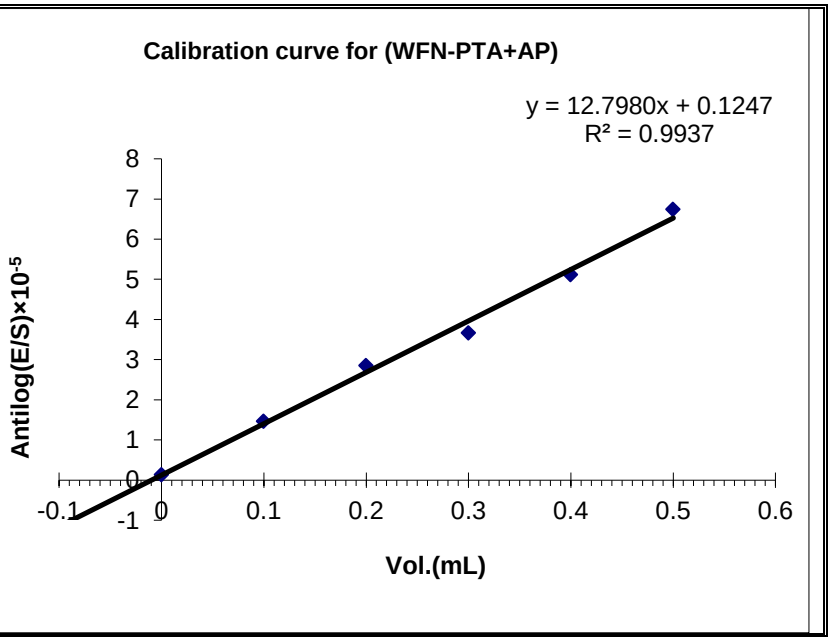


Figure (3.44): Antilog (E/S) versus the volume of the added standard for the determination of warfarin solution (10^{-4}M) by MSM using WFN-PTA+AP electrode

WFN- PTA+ DOPH Slope =26.00 Reading	
V(ml)	Antilog(E/S)
0	1.026×10^{1}
0.1	2.048×10^{1}
0.2	3.052×10^{1}
0.3	4.198×10^{1}
0.4	4.923×10^{1}
0.5	6.198×10^{1}

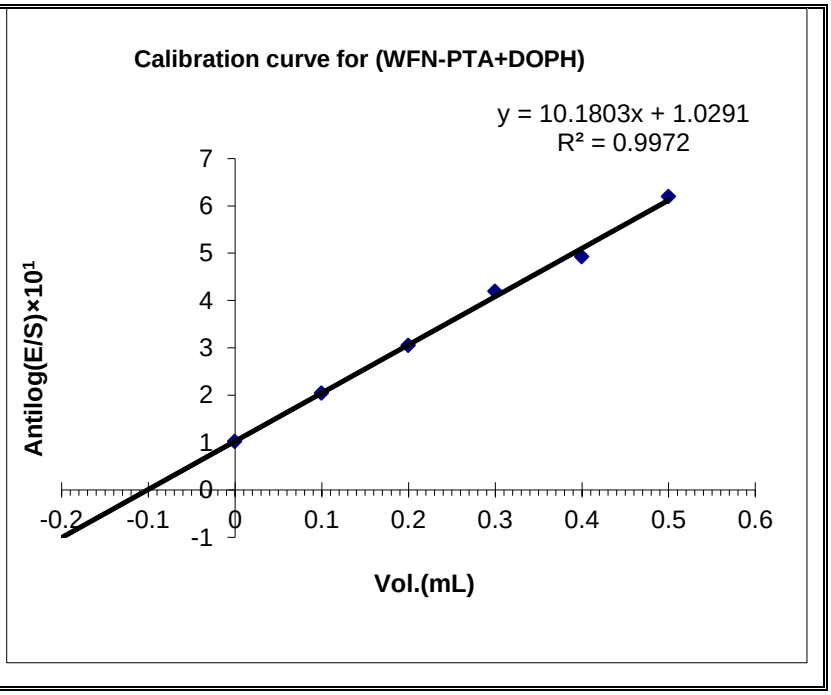


Figure (3.45): Antilog (E/S) versus the volume of the added standard for the determination of warfarin solution (10^{-3}M) by MSM using WFN-PTA+DOPH electrode

WFN- PTA+ DOPH Slope =26.00 Reading	
V(ml)	Antilog(E/S)
0	0.110×10^{1}
0.1	1.215×10^{1}
0.2	2.360×10^{1}
0.3	3.305×10^{1}
0.4	4.546×10^{1}
0.5	5.623×10^{1}

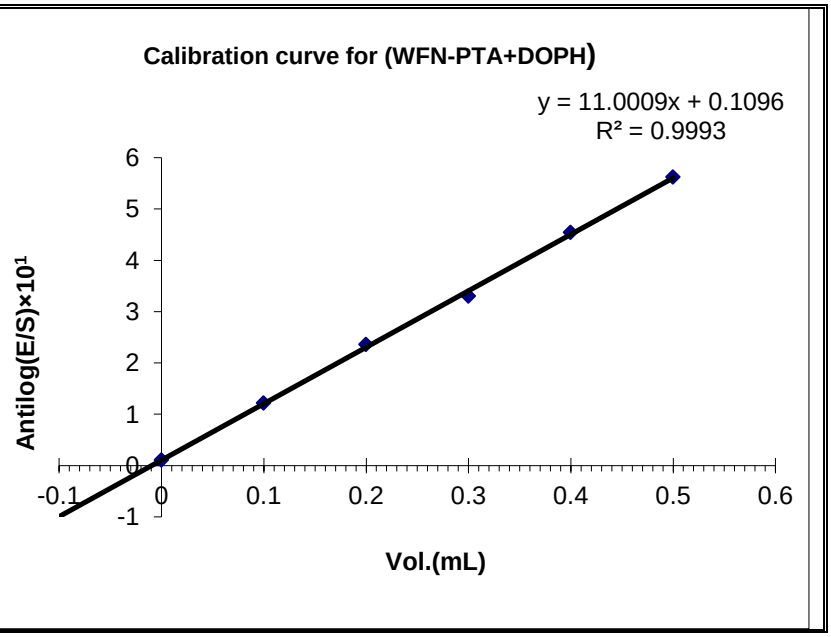


Figure (3.46): Antilog (E/S) versus the volume of the added standard for the determination of warfarin solution (10^{-4}M) by MSM using WFN-PTA+DOPH electrode

Table (3.38): The linear equations of the calibration curves for MSM, and correlation coefficients, volume at intercept with X axis and the concentration (C_U) for WFN-MPA electrodes.

Membrane composition	Concentration M	Linear equation	R^2	R	Volume at intercept (mL)	C_U M
WFN-MPA+OA	1.000×10^{-3}	Y = 17.1443x + 1.6911	0.9996	0.9998	0.0986	0.986×10^{-3}
	1.000×10^{-4}	Y = 17.9800x + 0.1767	0.9990	0.9995	0.0098	0.982×10^{-4}
WFN-MPA+TBP	1.000×10^{-3}	Y = 4.6114x + 0.4691	0.9990	0.9995	0.1017	1.017×10^{-3}
	1.000×10^{-4}	Y = 4.7871x + 0.0480	0.9992	0.9996	0.01002	1.002×10^{-4}
WFN-MPA+NB	1.000×10^{-3}	Y = 14.9649x + 1.4486	0.9982	0.9991	0.0967	0.967×10^{-3}
	1.000×10^{-4}	Y= 15.0274x + 0.1495	0.9980	0.9990	0.0099	0.994×10^{-4}
WFN-MPA+AP	1.000×10^{-3}	Y= 10.7329x + 1.0973	0.9992	0.9996	0.1022	1.022×10^{-3}
	1.000×10^{-4}	Y = 12.9911x + 0.1297	0.9992	0.9996	0.0099	0.998×10^{-4}
WFN-MPA+DOPH	1.000×10^{-3}	Y = 8.5800x + 0.8440	0.9990	0.9995	0.0983	0.983×10^{-3}
	1.000×10^{-4}	Y = 8.7720x + 0.0887	0.9996	0.9998	0.0101	1.011×10^{-4}

Table (3.39): The linear equations of the calibration curves for MSM, and correlation coefficients, volume at intercept with X axis and the concentration (C_U) for WFN-PTA electrodes.

Membrane composition	Concentration M	Linear equation	R^2	R	Volume at intercept (mL)	C_U M
WFN-PTA+OA	1.000×10^{-3}	y = 17.1149x + 1.6576	0.9976	0.9988	0.0968	0.968×10^{-3}
	1.000×10^{-4}	y = 15.5549x + 0.1583	0.9996	0.9998	0.0101	1.017×10^{-4}
WFN-PTA+TBP	1.000×10^{-3}	y = 3.1457x + 0.3069	0.9982	0.9991	0.0975	0.975×10^{-3}
	1.000×10^{-4}	y = 30.1269x + 0.2936	0.9954	0.9977	0.0097	0.974×10^{-4}
WFN-PTA+NB	1.000×10^{-3}	y = 4.5183x + 0.4581	0.9990	0.9995	0.1013	1.013×10^{-3}
	1.000×10^{-4}	y = 4.3206x + 0.0435	0.9996	0.9998	0.01006	1.006×10^{-4}
WFN-PTA+AP	1.000×10^{-3}	y = 13.2749x + 1.2973	0.9994	0.9997	0.0977	0.977×10^{-3}
	1.000×10^{-4}	y = 12.7980x + 0.1247	0.9936	0.9968	0.0097	0.974×10^{-4}
WFN-PTA+DOPH	1.000×10^{-3}	y = 10.1803x + 1.0291	0.9970	0.9985	0.1010	1.010×10^{-3}
	1.000×10^{-4}	y = 11.0009x + 0.1096	0.9992	0.9996	0.0099	0.996×10^{-4}

Table (3.40): Determination of warfarin sodium in the standard solutions using WFN-MPA electrode.

Membrane composition	Concentrations (M)			
	Sample	Measurements using potentiometric methods		
		Direct	SAM	MSA
WFN-MPA+OA	1×10^{-3}	0.951×10^{-3}	0.995×10^{-3}	0.986×10^{-3}
	RSD%	0.119*	2.150*	---
	RC%	95.1	99.5	98.6
	RE%	-4.9	-0.5	-1.4
	1×10^{-4}	0.983×10^{-4}	0.985×10^{-4}	0.982×10^{-4}
	RSD%	0.123	0.623*	---
	RC%	98.3	98.5	98.2
	RE%	-1.7	-1.5	-1.8
WFN-MPA+TBP	1×10^{-3}	0.959×10^{-3}	1.009×10^{-3}	1.017×10^{-3}
	RSD%	0.081*	0.886*	-
	RC%	95.9	100.9	101.7
	RE%	-4.1	0.9	1.7
	1×10^{-4}	0.953×10^{-4}	0.958×10^{-4}	$1.002\ 10^{-4}$
	RSD%	0.205*	0.849*	-
	RC%	95.3	95.8	100.2
	RE%	-4.7	-4.2	0.2
WFN-MPA +NB	1×10^{-3}	0.971×10^{-3}	1.015×10^{-3}	0.967×10^{-3}
	RSD%	0.295*	1.083*	-
	RC%	97.1	101.5	96.7
	RE%	-2.9	1.5	-3.3
	1×10^{-4}	0.978×10^{-4}	1.076×10^{-4}	0.994×10^{-4}
	RSD%	0.316*	1.251*	-
	RC%	97.8	107.6	99.4
	RE%	-2.2	7.6	-0.6
WFN-MPA+AP	1×10^{-3}	0.958×10^{-3}	1.005×10^{-3}	1.022×10^{-3}
	RSD%	0.748*	2.211*	---
	RC%	95.8	100.5	102.2
	RE%	-4.2	0.5	2.2
	1×10^{-4}	1.041×10^{-4}	0.948×10^{-4}	0.998×10^{-4}
	RSD%	2.454*	1.550*	---
	RC%	104.1	94.8	99.8
	RE%	4.1	-5.2	0.2
WFN-MPA+DOPH	1×10^{-3}	1.040×10^{-3}	0.986×10^{-3}	0.983×10^{-3}
	RSD%	0.114*	0.987*	----
	RC%	104.0	98.6	98.3
	RE%	4.0	-1.4	-1.7
	1×10^{-4}	1.043×10^{-3}	0.992×10^{-4}	1.011×10^{-4}
	RSD%	0.118*	0.938*	----
	RC%	104.3	99.2	101.1
	RE%	4.3	-0.8	1.1

*** Each measurement was repeated five times**

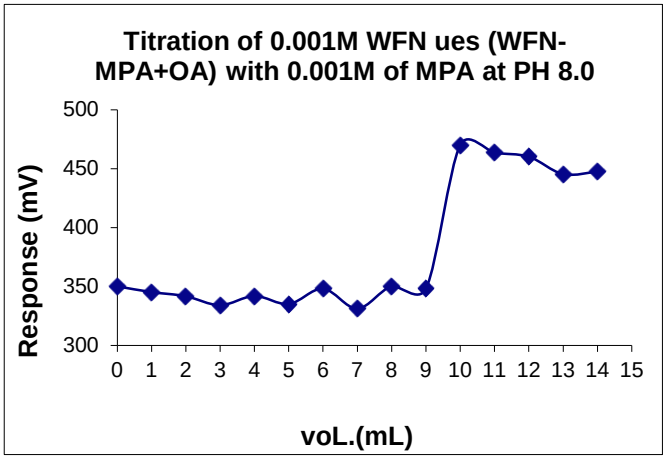
Table (3.41): Determination of warfarin sodium in the standard solutions using WFN-PTA electrode.

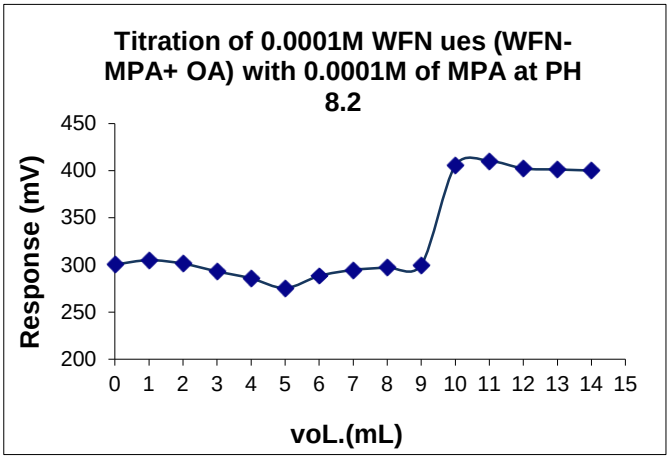
Membrane composition	Concentrations (M)			
	Sample	Measurements using potentiometric methods		
		Direct	SAM	MSA
WFN-PTA+OA	1×10^{-3}	1.047×10^{-3}	0.995×10^{-3}	0.968×10^{-3}
	RSD%	0.137*	1.971*	---
	RC%	104.7	99.5	96.8
	RE%	4.7	-0.5	-3.2
	1×10^{-4}	0.983×10^{-4}	1.037×10^{-4}	1.017×10^{-4}
	RSD%	0.364*	2.411*	---
	RC%	98.3	103.7	101.7
	RE%	-1.7	-3.7	-1.7
WFN-PTA+TBP	1×10^{-3}	1.017×10^{-3}	0.984×10^{-3}	0.975×10^{-3}
	RSD%	0.399*	1.542*	---
	RC%	101.7	98.4	97.5
	RE%	1.7	-1.6	-2.5
	1×10^{-4}	0.965×10^{-4}	0.979×10^{-4}	0.974×10^{-4}
	RSD%	0.899*	0.928*	---
	RC%	96.5	97.9	97.4
	RE%	-3.5	-2.1	-2.6
WFN-PTA +NB	1×10^{-3}	1.028×10^{-3}	0.989×10^{-3}	1.013×10^{-3}
	RSD%	0.338*	2.951*	---
	RC%	102.8	98.9	101.3
	RE%	2.8	-1.1	-1.3
	1×10^{-4}	0.956×10^{-4}	1.006×10^{-4}	1.006×10^{-4}
	RSD%	0.186*	1.721*	---
	RC%	95.6	100.6	100.6
	RE%	-4.4	0.6	0.6
WFN-PTA+AP	1×10^{-3}	0.969×10^{-3}	0.973×10^{-3}	0.977×10^{-3}
	RSD%	0.198*	1.536*	---
	RC%	96.9	97.3	97.7
	RE%	-3.1	-2.7	-2.3
	1×10^{-4}	0.965×10^{-4}	1.018×10^{-4}	0.974×10^{-4}
	RSD%	0.227*	1.745*	---
	RC%	96.5	101.8	97.4
	RE%	-3.5	1.8	-2.6
WFN-PTA+DOPH	1×10^{-3}	0.953×10^{-3}	0.997×10^{-3}	1.010×10^{-3}
	RSD%	0.435*	1.891*	----
	RC%	95.3	99.7	101.0
	RE%	-4.7	-0.3	1
	1×10^{-4}	1.028×0^{-3}	0.999×10^{-4}	0.996×10^{-4}
	RSD%	3.991*	1.743*	----
	RC%	102.8	99.9	99.6
	RE%	-2.8	-0.1	-0.4

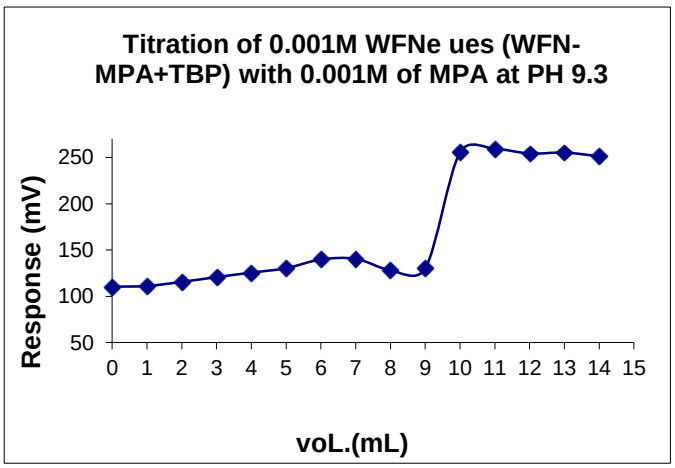
*** Each measurement was repeated five times**

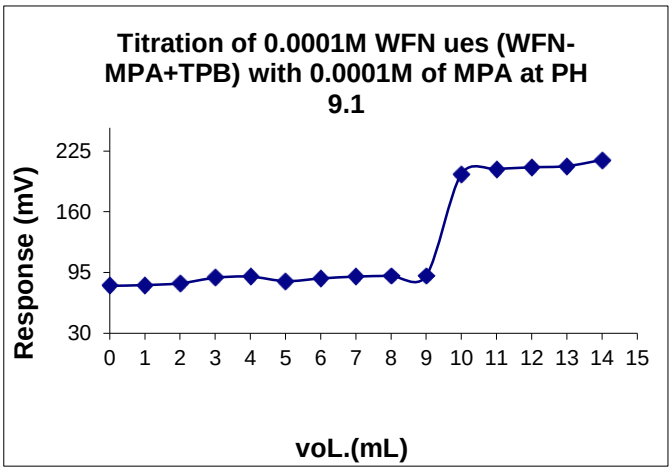
3.7.3. Titration method:

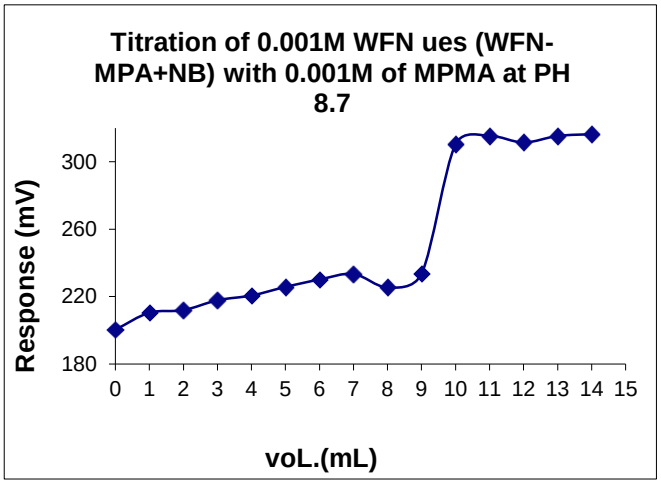
The principle of ion selective electrode titrations is based on the fact that in a stoichiometric reaction between two species in solution, the end point of the reaction is characterized by the total disappearance of one of the species or first appearance of a product of the reaction. Figure (3.47) , (3.48) show the titration curves of (10^{-3} and 10^{-4})M of Warfarin sodium solution with molybdo Phosphoric acid and phosphotungestic acid ,respectively as a ligand solution. The RSD% , RC% and RE % were calculate and the results obtained for each method are given in Tables (3.42) and (3.43) forWFN-MPA and WFN-MPA, respectively.

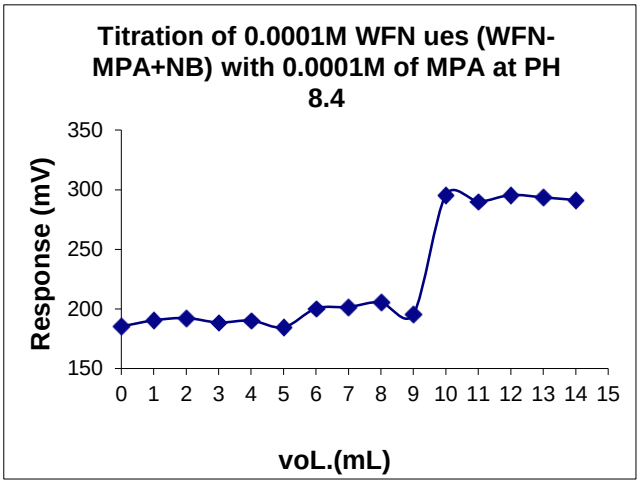


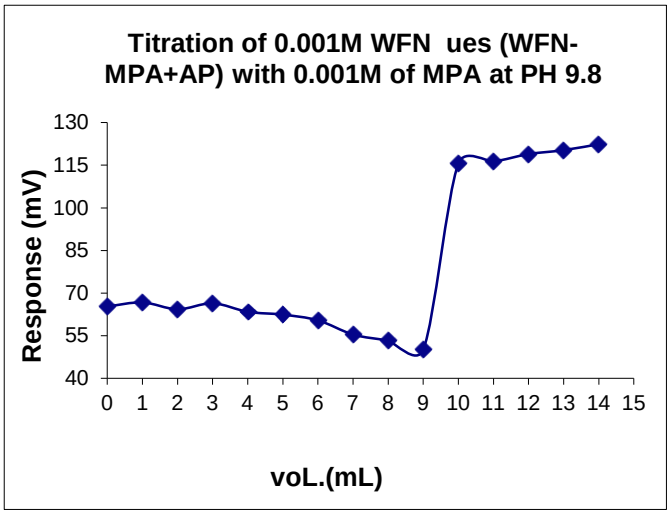


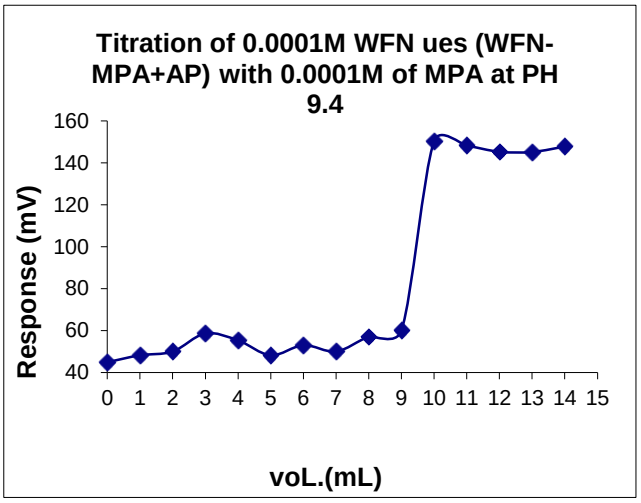


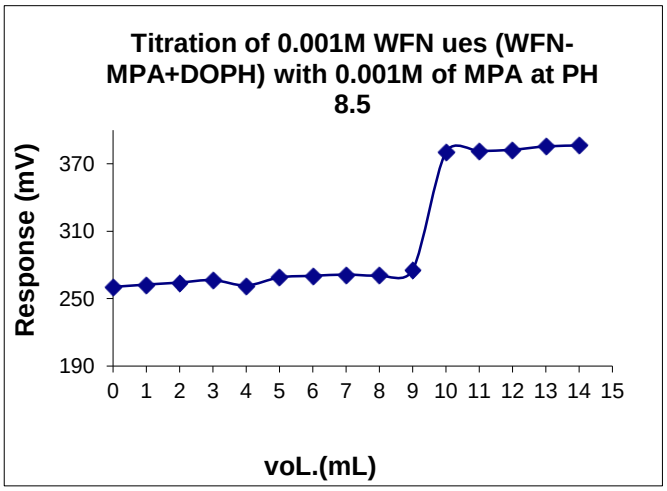












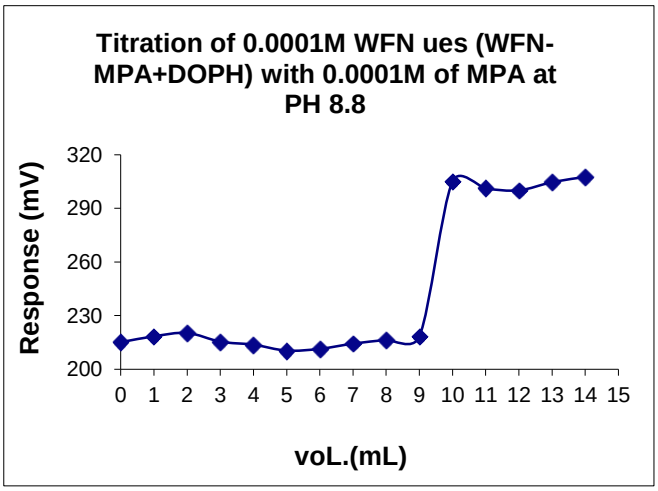
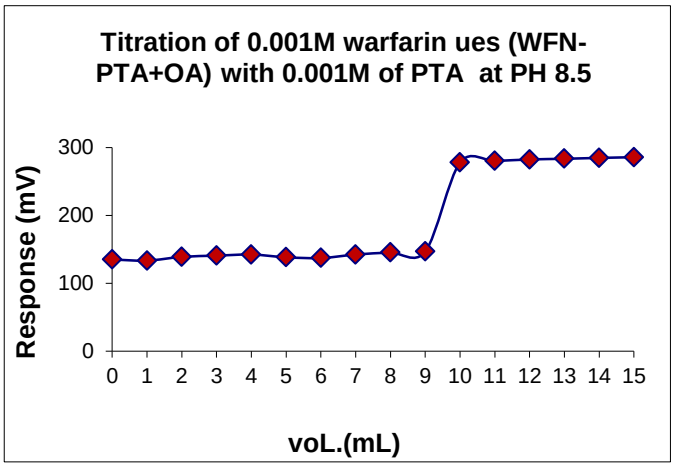
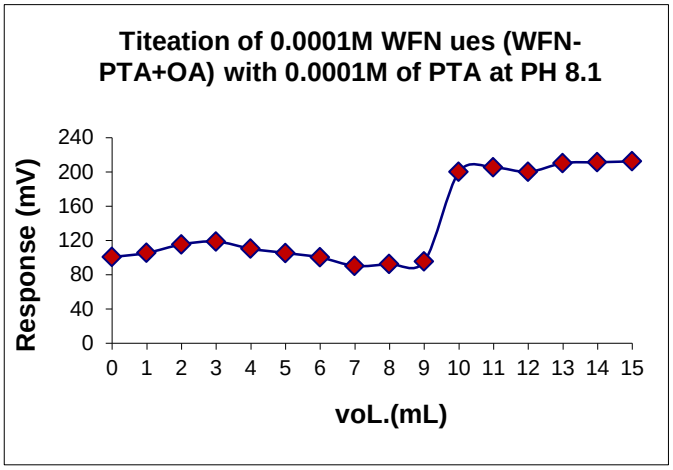
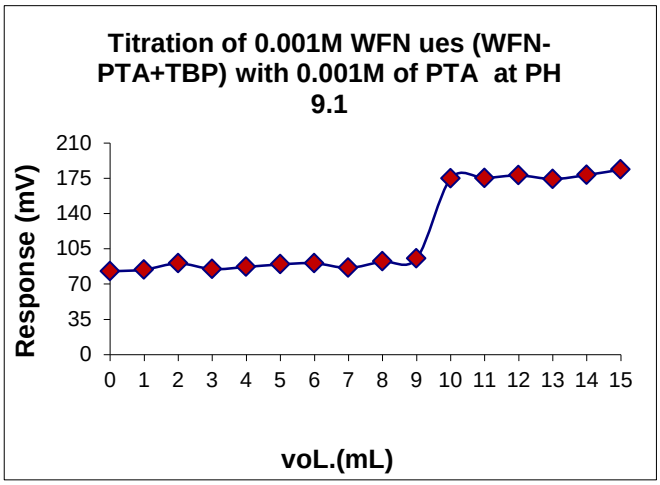
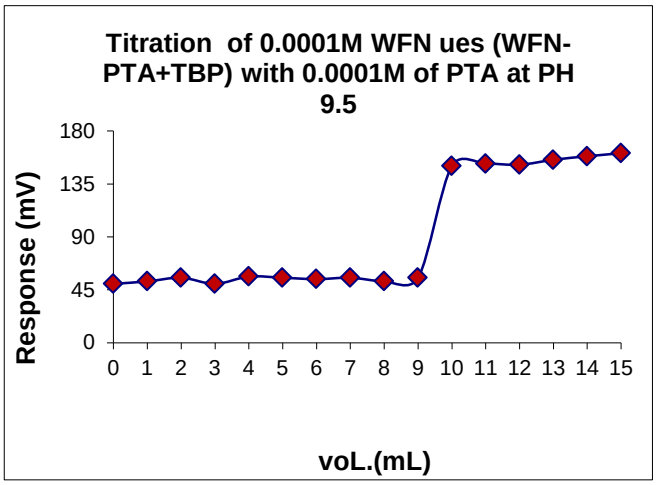


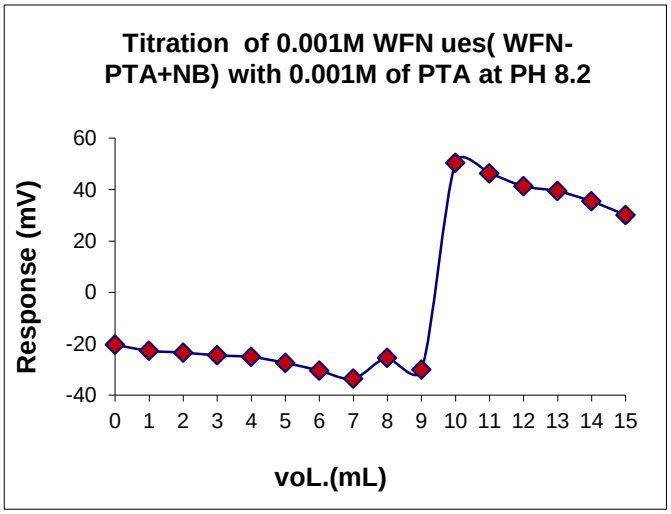
Figure (3.47) Titration curve for (10^{-3}, 10^{-4}) M of warfarin sodium solution by using MPA as a titrant .

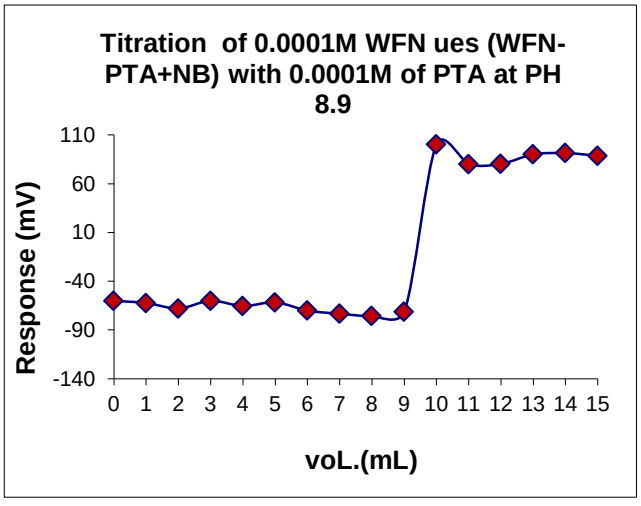

Titration of 0.001M warfarin ues (WFN-PTA+OA) with 0.001M of PTA at PH 8.5
Response (mV)
300
200
100
0
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
voL.(mL)


Titeation of 0.0001M WFN ues (WFN-PTA+OA) with 0.0001M of PTA at PH 8.1
Response (mV)
240
200
160
120
80
40
0
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
voL.(mL)


Titration of 0.001M WFN ues (WFN-PTA+TBP) with 0.001M of PTA at PH 9.1
Response (mV)
210
175
140
105
70
35
0
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
voL.(mL)


Titration of 0.0001M WFN ues (WFN-PTA+TBP) with 0.0001M of PTA at PH 9.5
Response (mV)
180
135
90
45
0
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
voL.(mL)


Titration of 0.001M WFN ues(WFN-PTA+NB) with 0.001M of PTA at PH 8.2
Response (mV)
60
40
20
0
-20
-40
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
voL.(mL)


Titration of 0.0001M WFN ues (WFN-PTA+NB) with 0.0001M of PTA at PH 8.9
Response (mV)
110
60
10
-40
-90
-140
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
voL.(mL)

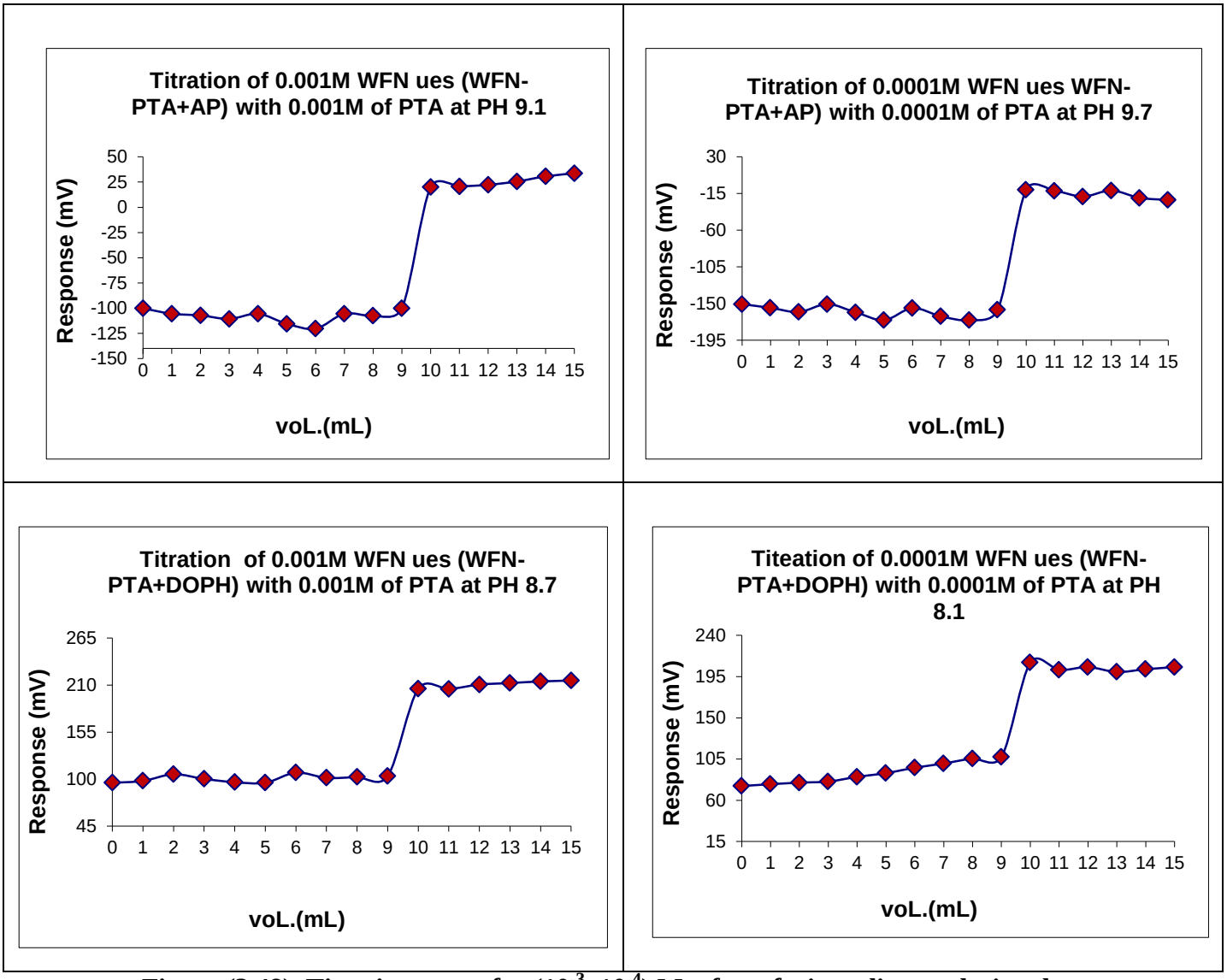


Figure (3.48) Titration curve for (10^{-3}, 10^{-4}) M of warfarin sodium solution by using PTA as a titrant .

Table (3.42): warfarin sodium standard solution analyses by using titration method for WFN-MPA electrodes.

Membrane Composition	Concentration (M)	
	Sample	**Measured using MPA as titrant**
WFN-MPA+ OA	1×10^{-3}	0.950×10^{-3}
	RSD%	0.856*
	RC%	95
	RE%	-5
	1×10^{-4}	0.975×10^{-4}
	RSD%	0.988*
	RC%	97.5
	RE%	-2.5
WFN-MPA + TBP	1×10^{-3}	0.955×10^{-3}
	RSD%	1.091*
	RC%	95.5
	RE%	-4.5
	1×10^{-4}	0.963×10^{-4}
	RSD%	1.323*
	RC%	96.3
	RE%	3.7
WFN-MPA+ NB	1×10^{-3}	0.945×10^{-3}
	RSD%	0.795*
	RC%	94.5
	RE%	-5.5
	1×10^{-4}	0.966×10^{-4}
	RSD%	0.995*
	RC%	96.6
	RE%	3.4

WFN-MPA+ AP	1×10^{-3}	0.953×10^{-3}
	RSD%	1.458*
	RC%	95.3
	RE%	-4.7
	1×10^{-4}	0.959×10^{-4}
	RSD%	2.122*
	RC%	95.9
	RE%	-4.5
WFN-MPA+DOPH	1×10^{-3}	0.971×10^{-3}
	RSD%	2.238*
	RC%	97.1
	RE%	-2.9
	1×10^{-4}	0.966×10^{-4}
	RSD%	2.165*
	RC%	96.6
	RE%	-3.4

Table (3.43): warfarin sodium standard solution analyses by using titration method for WFN-PTA electrodes.

Membrane Composition	**Concentration (M)**	
	Sample	**Measured using MPA as titrant**
WFN-PTA+ OA	1×10^{-3}	0.965×10^{-3}
	RSD%	0.955*
	RC%	96.5
	RE%	-3.5

WFN-PTA+ OA	1×10^{-4}	0.957×10^{-4}
	RSD%	0.874^{*}
	RC%	95.7
	RE%	-4.3
WFN-PTA + TBP	1×10^{-3}	0.975×10^{-3}
	RSD%	0.776^{*}
	RC%	97.5
	RE%	-2.5
	1×10^{-4}	0.947×10^{-4}
	RSD%	0.852^{*}
	RC%	94.7
	RE%	-5.3
WFN-PTA+ NB	1×10^{-3}	0.966×10^{-3}
	RSD%	1.195^{*}
	RC%	96.6
	RE%	-3.4
	1×10^{-4}	0.953×10^{-4}
	RSD%	1.015^{*}
	RC%	95.3
	RE%	-4.7
WFN-PTA+ AP	1×10^{-3}	0.970×10^{-3}
	RSD%	1.544^{*}
	RC%	97.0
	RE%	-3.0
	1×10^{-4}	0.957×10^{-4}
	RSD%	1.823^{*}
	RC%	95.7

	RE%	-4.3
WFN-PTA+DOPH	1×10^{-3}	0.960×10^{-3}
	RSD%	1.987*
	RC%	96.0
	RE%	-4.0
	1×10^{-4}	0.951×10^{-4}
	RSD%	2.045*
	RC%	95.1
	RE%	-4.9

*** Each measurement was repeated five times**

The calculated RSD% using titration method is relatively large in comparison with the other methods used. This may be attributed to the precipitation of (WFN-MPA) and (WFN-PTA) complexes on the surface of the membrane and poisoning the membrane. Also, the titration was carried out in neutral and acidic medium of warfarin sodium with molybdo Phosphoric acid and phosphoTungeston acid as a titrant solution we noticed that there is no response for warfarin electrodes. That means the electrodes are responsed in basic medium of drug.

3.8. Analytical application of the warfarin sodium electrodes:

The electrodes of (WFN-MPA) and (WFN-PTA) show the potentiometric responses when used to determination the warfarin sodium in pharmaceutical preparation by direct potentiometric method, standard addition method, multi addition method and potentiometric titration method the result shown from Tables (3.44) to (3.53) for (WFN-MPA) and (3.54) to (3.62) for (WFN-PTA) .

Table (3.44): Sample analyses of pharmaceutical Bristol (1mg) using WFN-MPA+ OA electrode

Pharmaceutical	Bristol (1mg)			
	Direct Method	SAM	MSA	Titration (MPA)
Concentration Prepared	1×10^{-3}	1×10^{-3}	1×10^{-3}	1×10^{-3}
*Found	0.949×10^{-3}	0.991×10^{-3}	0.982	0.950×10^{-3}
Recovery %	94.9	99.1	98.2	95.0
RE %	-5.1	-0.9	-1.8	-5.0
*RSD%	0.162*	0.882*	--	0.985*
Fexperimental	8.8	10.8		14.5
F theoretical	19.2			
Pharmaceutical	**Bristol (1mg)**			
	Direct Method	**SAM**	**MSA**	**Titration (MPA)**
Concentration Prepared	1×10^{-4}	1×10^{-4}	1×10^{-4}	1×10^{-4}
*Found	0.975×10^{-4}	0.994×10^{-4}	1.022×10^{-4}	0.970×10^{-4}
Recovery %	97.5	99.4	102.2	97.0
RE %	-2.5	-0.6	2.2	-3.0
*RSD%	0.153*	0.935*	--	1.045*
Fexperimental	10.5	13.7		15.8
F theoretical	19.2			

Table (3.45): Sample analyses of pharmaceutical Actavis (3 mg) using WFN-MPA+ OA electrode

Pharmaceutical	Actavis (3 mg)			
	Direct Method	SAM	MSA	Titration (MPA)
Concentration Prepared	1×10^{-3}	1×10^{-3}	1×10^{-3}	1×10^{-3}
*Found	0.950×10^{-3}	1.011×10^{-3}	1.021×10^{-3}	0.952×10^{-3}
Recovery %	95.0	101.1	102.1	95.2
RE %	-5.0	1.1	2.1	-4.8
*RSD%	0.157*	1.012*	--	1.033*
Fexperimental	11.2	6.8		7.8
F theoretical	19.2			
Pharmaceutical	**Actavis (3 mg)**			
	Direct Method	**SAM**	**MSA**	**Titration (MPA)**
Concentration Prepared	1×10^{-4}	1×10^{-4}	1×10^{-4}	1×10^{-4}
*Found	0.976×10^{-4}	1.010×10^{-4}	0.981×10^{-4}	0.968×10^{-4}
Recovery %	97.6	101	98.1	96.8
RE %	-2.4	1	1.9	-3.8
*RSD%	0.143*	0.835*	--	1.156*
Fexperimental	17.2	11.4		9.9
F theoretical	19.2			

Table (3.46): Sample analyses of pharmaceutical Bristol (1mg) using WFN-MPA+ TBP electrode

Pharmaceutical	**Bristol (1mg)**			
	Direct Method	**SAM**	**MSA**	**Titration (MPA)**
Concentration Prepared	**1×10^{-3}**	**1×10^{-3}**	**1×10^{-3}**	**1×10^{-3}**
***Found**	0.955×10^{-3}	0.970×10^{-3}	1.019×10^{-3}	0.953×10^{-3}
Recovery %	95.5	97.0	101.9	95.3
RE %	-4.5	-3.0	-1.9	-4.7
***RSD%**	0.113*	1.085*	--	0.995*
Fexperimental	12.3	8.7	--	6.6
F theoretical	19.2			
Pharmaceutical	**Bristol (1mg)**			
	Direct Method	**SAM**	**MSA**	**Titration (MPA)**
Concentration Prepared	**1×10^{-4}**	**1×10^{-4}**	**1×10^{-4}**	**1×10^{-4}**
***Found**	1.050×10^{-4}	0.963×10^{-4}	0.994×10^{-4}	0.960×10^{-4}
Recovery %	105.0	96.3	99.4	96.0
RE %	5.0	-3.7	-0.6	-4.0
***RSD%**	0.245*	0.988*	--	1.212*
Fexperimental	17.3	11.1	--	12.5
F theoretical	19.2			

Table (3.47): Sample analyses of pharmaceutical Actavis (3 mg) using WFN-MPA+ TBP electrode

Pharmaceutical	**Actavis (3 mg)**			
	Direct Method	**SAM**	**MSA**	**Titration (MPA)**
Concentration Prepared	**1×10^{-3}**	**1×10^{-3}**	**1×10^{-3}**	**1×10^{-3}**
***Found**	1.040×10^{-3}	1.029×10^{-3}	0.983×10^{-3}	0.951×10^{-3}
Recovery %	104.0	102.9	98.3	95.1
RE %	4.0	2.9	-1.7	-4.9
***RSD%**	0.231*	1.123*	--	1.081*
Fexperimental	11.5	13.5	--	10.5
F theoretical	19.2			
Pharmaceutical	**Actavis (3 mg)**			
	Direct Method	**SAM**	**MSA**	**Titration (MPA)**
Concentration Prepared	**1×10^{-4}**	**1×10^{-4}**	**1×10^{-4}**	**1×10^{-4}**
***Found**	1.048×10^{-4}	0.960×10^{-4}	0.991×10^{-4}	0.961×10^{-4}
Recovery %	104.8	96.0	99.1	96.1
RE %	4.8	-4.0	-0.9	-3.9
***RSD%**	0.438*	1.011*	--	1.355*
Fexperimental	16.8	14.8	--	13.7
F theoretical	19.2			

Table (3.48): Sample analyses of pharmaceutical Bristol (1mg) using WFN-MPA+ NB electrode

Pharmaceutical	Bristol (1mg)			
	Direct Method	SAM	MSA	Titration (MPA)
Concentration Prepared	1×10^{-3}	1×10^{-3}	1×10^{-3}	1×10^{-3}
*Found	0.970×10^{-3}	1.010×10^{-3}	0.962×10^{-3}	0.950×10^{-3}
Recovery %	97.0	101.0	96.2	95.0
RE %	-3.0	1.0	-3.8	-5.0
*RSD%	0.311*	1.235*	--	0.838*
Fexperimental	8.1	10.4	--	6.6
F theoretical	19.2			
Pharmaceutical	Bristol (1mg)			
	Direct Method	SAM	MSA	Titration (MPA)
Concentration Prepared	1×10^{-4}	1×10^{-4}	1×10^{-4}	1×10^{-4}
*Found	0.973×10^{-4}	0.986×10^{-4}	1.010×10^{-4}	0.961×10^{-4}
Recovery %	97.3	98.6	101.0	96.1
RE %	-2.7	-1.4	1.0	-3.9
*RSD%	0.241*	1.221*	--	1.023*
Fexperimental	11.7	16.3	--	11.4
F theoretical	19.2			

Table (3.49): Sample analyses of pharmaceutical Actavis (3 mg) using WFN-MPA+ NB electrode

Pharmaceutical	**Actavis (3 mg)**			
	Direct Method	**SAM**	**MSA**	**Titration (MPA)**
Concentration Prepared	**1×10^{-3}**	**1×10^{-3}**	**1×10^{-3}**	**1×10^{-3}**
***Found**	0.969×10^{-3}	0.992×10^{-3}	0.966×10^{-3}	0.950×10^{-3}
Recovery %	96.9	99.2	96.6	95.0
RE %	-3.1	-0.8	-3.4	-5
***RSD%**	0.315*	1.102*	--	0.854*
Fexperimental	11.3	7.6	--	8.5
F theoretical	19.2			
Pharmaceutical	**Actavis (3 mg)**			
	Direct Method	**SAM**	**MSA**	**Titration (MPA)**
Concentration Prepared	**1×10^{-4}**	**1×10^{-4}**	**1×10^{-4}**	**1×10^{-4}**
***Found**	1.025×10^{-4}	1.015×10^{-4}	0.992×10^{-4}	0.960×10^{-4}
Recovery %	102.5	101.5	99.2	96.0
RE %	2.5	1.5	-0.8	-4.0
***RSD%**	0.285*	1.122*	--	1.123*
Fexperimental	13.6	12.1	--	13.4
F theoretical	19.2			

Table (3.50): Sample analyses of pharmaceutical Bristol (1mg) using WFN-MPA+ AP electrode

Pharmaceutical	Bristol (1mg)			
	Direct Method	SAM	MSA	Titration (MPA)
Concentration Prepared	1×10^{-3}	1×10^{-3}	1×10^{-3}	1×10^{-3}
*Found	0.953×10^{-3}	1.032×10^{-3}	1.025×10^{-3}	0.951×10^{-3}
Recovery %	95.3	103.2	102.5	95.1
RE %	-4.7	-3.2	2.5	-4.9
*RSD%	0.977*	2.123*	--	2.013*
Fexperimental	15.3	7.7	--	11.3
F theoretical	19.2			
Pharmaceutical	Bristol (1mg)			
	Direct Method	SAM	MSA	Titration (MPA)
Concentration Prepared	1×10^{-4}	1×10^{-4}	1×10^{-4}	1×10^{-4}
*Found	1.050×10^{-4}	1.028×10^{-4}	1.008×10^{-4}	0.955×10^{-4}
Recovery %	105.0	102.8	100.8	95.5
RE %	5.0	2.8	0.8	-5.5
*RSD%	2.231*	1.575*	--	2.555*
Fexperimental	18.3	11.1	--	14.7
F theoretical	19.2			

Table (3.51): Sample analyses of pharmaceutical Actavis (3 mg) using WFN-MPA+ AP electrode

Pharmaceutical	Actavis (3 mg)			
	Direct Method	SAM	MSA	Titration (MPA)
Concentration Prepared	1×10^{-3}	1×10^{-3}	1×10^{-3}	1×10^{-3}
*Found	1.043×10^{-3}	0.963×10^{-3}	0.977×10^{-3}	0.950×10^{-3}
Recovery %	104.3	96.3	97.7	95.0
RE %	4.3	-3.7	-2.3	5.0
*RSD%	1.034*	2.351*	--	1.853*
Fexperimental	10.1	12.3	--	7.1
F theoretical	19.2			
Pharmaceutical	Actavis (3 mg)			
	Direct Method	SAM	MSA	Titration (MPA)
Concentration Prepared	1×10^{-4}	1×10^{-4}	1×10^{-4}	1×10^{-4}
*Found	1.045×10^{-4}	0.970×10^{-4}	0.995×10^{-4}	0.953×10^{-4}
Recovery %	104.5	97.0	99.5	95.3
RE %	4.5	-3.0	0.5	-4.7
*RSD%	1.133*	1.225*	--	2.831*
Fexperimental	12.5	16.4	--	9.8
F theoretical	19.2			

Table (3.52): Sample analyses of pharmaceutical Bristol (1mg) using WFN-MPA+ DOPH electrode

Pharmaceutical	Bristol (1mg)			
	Direct Method	SAM	MSA	Titration (MPA)
Concentration Prepared	1×10^{-3}	1×10^{-3}	1×10^{-3}	1×10^{-3}
*Found	0.954×10^{-3}	0.990×10^{-3}	1.020×10^{-3}	0.970×10^{-3}
Recovery %	95.4	99.0	102.0	97.0
RE %	-4.6	-1.0	2	-3.0
*RSD%	0.133*	1.034*	--	2.573*
Fexperimental	13.8	5.8	--	14.3
F theoretical	19.2			
Pharmaceutical	**Bristol (1mg)**			
	Direct Method	**SAM**	**MSA**	**Titration (MPA)**
Concentration Prepared	1×10^{-4}	1×10^{-4}	1×10^{-4}	1×10^{-4}
*Found	0.960×10^{-4}	1.027×10^{-4}	0.985×10^{-4}	0.965×10^{-4}
Recovery %	96.0	102.7	98.5	96.5
RE %	-4.0	2.7	-1.5	-3.5
*RSD%	0.187*	0.993*	--	-2.217*
Fexperimental	17.7	8.9	--	18.1
F theoretical	19.2			

Table (3.53): Sample analyses of pharmaceutical Actavis (3 mg) using WFN-MPA+ DOPH electrode

Pharmaceutical	**Actavis (3 mg)**			
	Direct Method	**SAM**	**MSA**	**Titration (MPA)**
Concentration Prepared	**1×10^{-3}**	**1×10^{-3}**	**1×10^{-3}**	**1×10^{-3}**
***Found**	1.043×10^{-3}	1.009×10^{-3}	0.980×10^{-3}	0.970×10^{-3}
Recovery %	104.3	100.9	98.0	97.0
RE %	4.3	0.9	-2.0	-3.0
***RSD%**	0.314*	1.053*	--	2.217*
Fexperimental	**11.8**	**12.8**	**--**	**18.1**
F theoretical	**19.2**			
Pharmaceutical	**Actavis (3 mg)**			
	Direct Method	**SAM**	**MSA**	**Titration (MPA)**
Concentration Prepared	**1×10^{-4}**	**1×10^{-4}**	**1×10^{-4}**	**1×10^{-4}**
***Found**	0.958×10^{-4}	0.975×10^{-4}	1.017×10^{-4}	0.963×10^{-4}
Recovery %	95.8	97.5	101.7	96.3
RE %	-4.2	-2.5	1.7	-3.7
***RSD%**	0.213*	0.989*	--	2.313*
Fexperimental	15.7	17.3	--	12.6
F theoretical	19.2			

* Each measurement was repeated three times.

Table (3.54): Sample analyses of pharmaceutical Bristol (1mg) using WFN-PTA+ OA electrode

Pharmaceutical	Bristol (1mg)			
	Direct Method	SAM	MSA	Titration (MPA)
Concentration Prepared	1×10^{-3}	1×10^{-3}	1×10^{-3}	1×10^{-3}
*Found	1.050×10^{-3}	0.991×10^{-3}	1.035×10^{-3}	0.960×10^{-3}
Recovery %	105.0	99.1	103.5	96.0
RE %	5.0	-0.9	-3.5	-4.0
*RSD%	0.337*	2.011*	--	1.033*
Fexperimental	9.3	11.3	--	7.5
F theoretical	19.2			
Pharmaceutical	**Bristol (1mg)**			
	Direct Method	**SAM**	**MSA**	**Titration (MPA)**
Concentration Prepared	1×10^{-4}	1×10^{-4}	1×10^{-4}	1×10^{-4}
*Found	1.023×10^{-4}	0.963×10^{-4}	0.981×10^{-4}	0.950×10^{-4}
Recovery %	102.3	96.3	98.1	95.0
RE %	2.3	-3.7	-1.9	-5.0
*RSD%	0.577*	2.613*	--	0.938*
Fexperimental	12.8	13.1	--	10.3
F theoretical	19.2			

Table (3.55): Sample analyses of pharmaceutical Actavis (3 mg) using WFN-PTA+ OA electrode

Pharmaceutical	Actavis (3 mg)			
	Direct Method	SAM	MSA	Titration (MPA)
Concentration Prepared	1×10^{-3}	1×10^{-3}	1×10^{-3}	1×10^{-3}
*Found	0.953×10^{-3}	1.010×10^{-3}	1.033×10^{-3}	0.955×10^{-3}
Recovery %	95.3	101.0	103.3	95.5
RE %	-4.7	1.0	3.3	-4.5
*RSD%	0.478*	2.103*	--	1.123*
Fexperimental	11.1	10.8	--	11.8
F theoretical	19.2			
Pharmaceutical	**Actavis (3 mg)**			
	Direct Method	**SAM**	**MSA**	**Titration (MPA)**
Concentration Prepared	1×10^{-4}	1×10^{-4}	1×10^{-4}	1×10^{-4}
*Found	0.975×10^{-4}	1.040×10^{-4}	1.021×10^{-4}	0.953×10^{-4}
Recovery %	97.5	104.0	102.1	95.3
RE %	-2.5	4.0	2.1	-4.7
*RSD%	0.713*	2.533*	--	1.021*
Fexperimental	8.8	12.4	--	11.2
F theoretical	19.2			

Table (3.56): Sample analyses of pharmaceutical Bristol (1mg) using WFN-PTA+ TBP electrode

Pharmaceutical	Bristol (1mg)			
	Direct Method	SAM	MSA	Titration (MPA)
Concentration Prepared	1×10^{-3}	1×10^{-3}	1×10^{-3}	1×10^{-3}
*Found	0.980×10^{-3}	1.020×10^{-3}	0.970×10^{-3}	0.970×10^{-3}
Recovery %	98.0	102.0	97.0	97.0
RE %	-2.0	2.0	-3	-3
*RSD%	0.738*	1.857*	--	1.034*
Fexperimental	10.4	13.1	--	14.3
F theoretical	19.2			
Pharmaceutical	**Bristol (1mg)**			
	Direct Method	**SAM**	**MSA**	**Titration (MPA)**
Concentration Prepared	1×10^{-4}	1×10^{-4}	1×10^{-4}	1×10^{-4}
*Found	1.040×10^{-4}	0.973×10^{-4}	1.030×10^{-4}	0.950×10^{-4}
Recovery %	104.0	97.3	103.0	95.0
RE %	4.0	-2.7	3.0	-5.0
*RSD%	0.975*	1.025*	--	1.055*
Fexperimental	11.5	12.5	--	15.1
F theoretical	19.2			

Table (3.57): Sample analyses of pharmaceutical Actavis (3 mg) using WFN-PTA+ TBP electrode

Pharmaceutical	Actavis (3 mg)			
	Direct Method	SAM	MSA	Titration (MPA)
Concentration Prepared	1×10^{-3}	1×10^{-3}	1×10^{-3}	1×10^{-3}
*Found	1.021×10^{-3}	0.979×10^{-3}	1.028×10^{-3}	0.965×10^{-3}
Recovery %	102.1	97.9	102.8	96.5
RE %	2.1	-2.1	2.8	-3.5
*RSD%	0.811*	1.981*	--	1.191*
Fexperimental	9.5	14.5	--	15.7
F theoretical	19.2			
Pharmaceutical	**Actavis (3 mg)**			
	Direct Method	**SAM**	**MSA**	**Titration (MPA)**
Concentration Prepared	1×10^{-4}	1×10^{-4}	1×10^{-4}	1×10^{-4}
*Found	1.038×10^{-4}	1.021×10^{-4}	0.971×10^{-4}	0.950×10^{-4}
Recovery %	103.8	102.1	97.1	95.0
RE %	3.8	2.1	-2.9	-5.0
*RSD%	0.993*	1.103*	--	1.103*
Fexperimental	9.8	11.4	--	16.3
F theoretical	19.2			

Table (3.58): Sample analyses of pharmaceutical Bristol (1mg) using WFN-PTA+ NB electrode

Pharmaceutical	Bristol (1mg)			
	Direct Method	SAM	MSA	Titration (MPA)
Concentration Prepared	1×10^{-3}	1×10^{-3}	1×10^{-3}	1×10^{-3}
*Found	0.971×10^{-3}	1.012×10^{-3}	0.982×10^{-3}	0.961×10^{-3}
Recovery %	97.1	101.2	98.2	96.1
RE %	-2.9	1.2	-1.8	-3.9
*RSD%	0.735*	2.973*	--	1.199
Fexperimental	17.3	8.5	--	14.5
F theoretical	19.2			
Pharmaceutical	**Bristol (1mg)**			
	Direct Method	**SAM**	**MSA**	**Titration (MPA)**
Concentration Prepared	1×10^{-4}	1×10^{-4}	1×10^{-4}	1×10^{-4}
*Found	0.953×10^{-4}	0.992×10^{-4}	1.009×10^{-4}	0.950×10^{-4}
Recovery %	95.3	99.2	100.9	95.0
RE %	-4.7	-0.8	0.9	-5.0
*RSD%	0.573*	1.937*	--	1.113*
Fexperimental	11.3	13.7	--	12.8
F theoretical	19.2			

Table (3.59): Sample analyses of pharmaceutical Actavis (3 mg) using WFN-PTA+ NB electrode

Pharmaceutical	Actavis (3 mg)			
	Direct Method	SAM	MSA	Titration (MPA)
Concentration Prepared	1×10^{-3}	1×10^{-3}	1×10^{-3}	1×10^{-3}
*Found	0.969×10^{-3}	0.981×10^{-3}	1.019×10^{-3}	0.965×10^{-3}
Recovery %	96.9	98.1	101.9	96.5
RE %	-3.1	-1.9	1.9	-3.5
*RSD%	0.851*	2.879*	--	1.211*
Fexperimental	15.9	10.3	--	16.1
F theoretical	19.2			
Pharmaceutical	**Actavis (3 mg)**			
	Direct Method	**SAM**	**MSA**	**Titration (MPA)**
Concentration Prepared	1×10^{-4}	1×10^{-4}	1×10^{-4}	1×10^{-4}
*Found	1.049×10^{-4}	0.995×10^{-4}	0.992×10^{-4}	0.953×10^{-4}
Recovery %	104.9	99.5	99.2	95.3
RE %	4.9	-0.5	-0.8	-4.7
*RSD%	0.612*	2.911*	--	1.147*
Fexperimental	12.7	12.1	--	11.7
F theoretical	19.2			

Table (3.60): Sample analyses of pharmaceutical Bristol (1mg) using WFN-PTA+ AP electrode

Pharmaceutical	Bristol (1mg)			
	Direct Method	SAM	MSA	Titration (MPA)
Concentration Prepared	1×10^{-3}	1×10^{-3}	1×10^{-3}	1×10^{-3}
*Found	0.965×10^{-3}	0.970×10^{-3}	1.024×10^{-3}	0.955×10^{-3}
Recovery %	96.5	97.0	102.4	95.5
RE %	-3.5	-3.0	2.4	-4.5
*RSD%	0.237*	1.671*	--	2.132*
Fexperimental	15.2	11.8	--	16.1
F theoretical	19.2			
Pharmaceutical	**Bristol (1mg)**			
	Direct Method	**SAM**	**MSA**	**Titration (MPA)**
Concentration Prepared	1×10^{-4}	1×10^{-4}	1×10^{-4}	1×10^{-4}
*Found	1.035×10^{-4}	1.021×10^{-4}	0.970×10^{-4}	0.965×10^{-4}
Recovery %	103.5	102.1	97.0	96.5
RE %	3.5	2.1	-3.0	-3.5
*RSD%	0.537*	1.933*	--	1.873*
Fexperimental	13.7	8.7	--	13.3
F theoretical	19.2			

Table (3.61): Sample analyses of pharmaceutical Actavis (3 mg) using WFN-PTA+ AP electrode

Pharmaceutical	Actavis (3 mg)			
	Direct Method	SAM	MSA	Titration (MPA)
Concentration Prepared	1×10^{-3}	1×10^{-3}	1×10^{-3}	1×10^{-3}
*Found	1.032×10^{-3}	0.972×10^{-3}	0.974×10^{-3}	0.963×10^{-3}
Recovery %	103.2	97.2	97.4	96.3
RE %	3.2	-2.8	-2.6	-3.7
*RSD%	0.274*	1.637*	--	1.985*
Fexperimental	14.7	11.5	--	13.1
F theoretical	19.2			
Pharmaceutical	**Actavis (3 mg)**			
	Direct Method	**SAM**	**MSA**	**Titration (MPA)**
Concentration Prepared	1×10^{-4}	1×10^{-4}	1×10^{-4}	1×10^{-4}
*Found	1.036×10^{-4}	0.980×10^{-4}	0.973×10^{-4}	0.950×10^{-4}
Recovery %	103.6	98.0	97.3	95.0
RE %	3.6	2.0	-2.7	-5.0
*RSD%	0.578*	1.917*	--	2.220
Fexperimental	14.8	10.9	--	12.5
F theoretical	19.2			

Table (3.62): Sample analyses of pharmaceutical Bristol (1mg) using WFN-PTA+ DOPH electrode

Pharmaceutical	Bristol (1mg)			
	Direct Method	SAM	MSA	Titration (MPA)
Concentration Prepared	1×10^{-3}	1×10^{-3}	1×10^{-3}	1×10^{-3}
*Found	1.050×10^{-3}	1.004×10^{-3}	1.020×10^{-3}	0.955×10^{-3}
Recovery %	105.0	100.4	102.0	95.5
RE %	5.0	0.4	2	-4.5
*RSD%	0.616*	1.976*	--	2.213*
Fexperimental	17.3	9.7	--	11.3
F theoretical	19.2			
Pharmaceutical	**Bristol (1mg)**			
	Direct Method	**SAM**	**MSA**	**Titration (MPA)**
Concentration Prepared	1×10^{-4}	1×10^{-4}	1×10^{-4}	1×10^{-4}
*Found	0.970×10^{-4}	0.995×10^{-4}	1.007×10^{-4}	0.950×10^{-4}
Recovery %	97.0	99.5	100.7	95.0
RE %	-3	-0.5	0.7	-5.0
*RSD%	3.313*	1.911*	--	2.514*
Fexperimental	15.1	10.8	--	13.3
F theoretical	19.2			

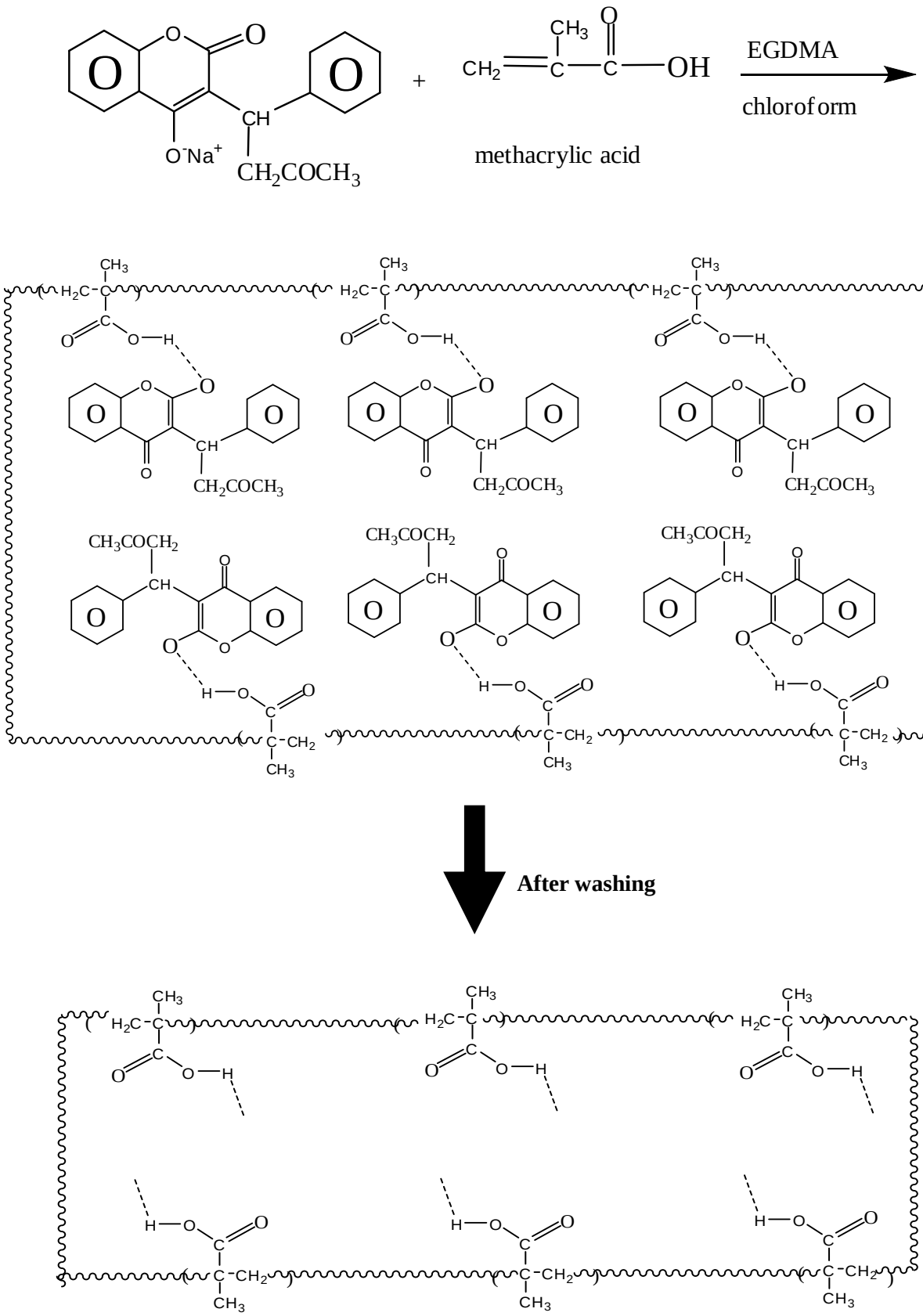
Table (3.63): Sample analyses of pharmaceutical Actavis (3 mg) using WFN-PTA+ DOPH electrode

Pharmaceutical	Actavis (3 mg)			
	Direct Method	SAM	MSA	Titration (MPA)
Concentration Prepared	1×10^{-3}	1×10^{-3}	1×10^{-3}	1×10^{-3}
*Found	0.952	0.991×10^{-3}	0.985×10^{-3}	0.957×10^{-3}
Recovery %	95.2	99.1	98.5	95.7
RE %	-4.8	-0.9	-1.5	-4.3
*RSD%	0.723*	1.893*	--	2.199*
Fexperimental	16.4	10.4	--	11.7
F theoretical	19.2			
Pharmaceutical	**Actavis (3 mg)**			
	Direct Method	**SAM**	**MSA**	**Titration (MPA)**
Concentration Prepared	1×10^{-4}	1×10^{-4}	1×10^{-4}	1×10^{-4}
*Found	1.031×10^{-4}	1.005×10^{-4}	0.992×10^{-4}	0.951×10^{-4}
Recovery %	103.1	100.5	99.2	95.1
RE %	3.1	0.5	-0.8	-4.9
*RSD%	3.987*	2.012*	--	2.177*
Fexperimental	15.8	11.3	--	14.5
F theoretical	19.2			

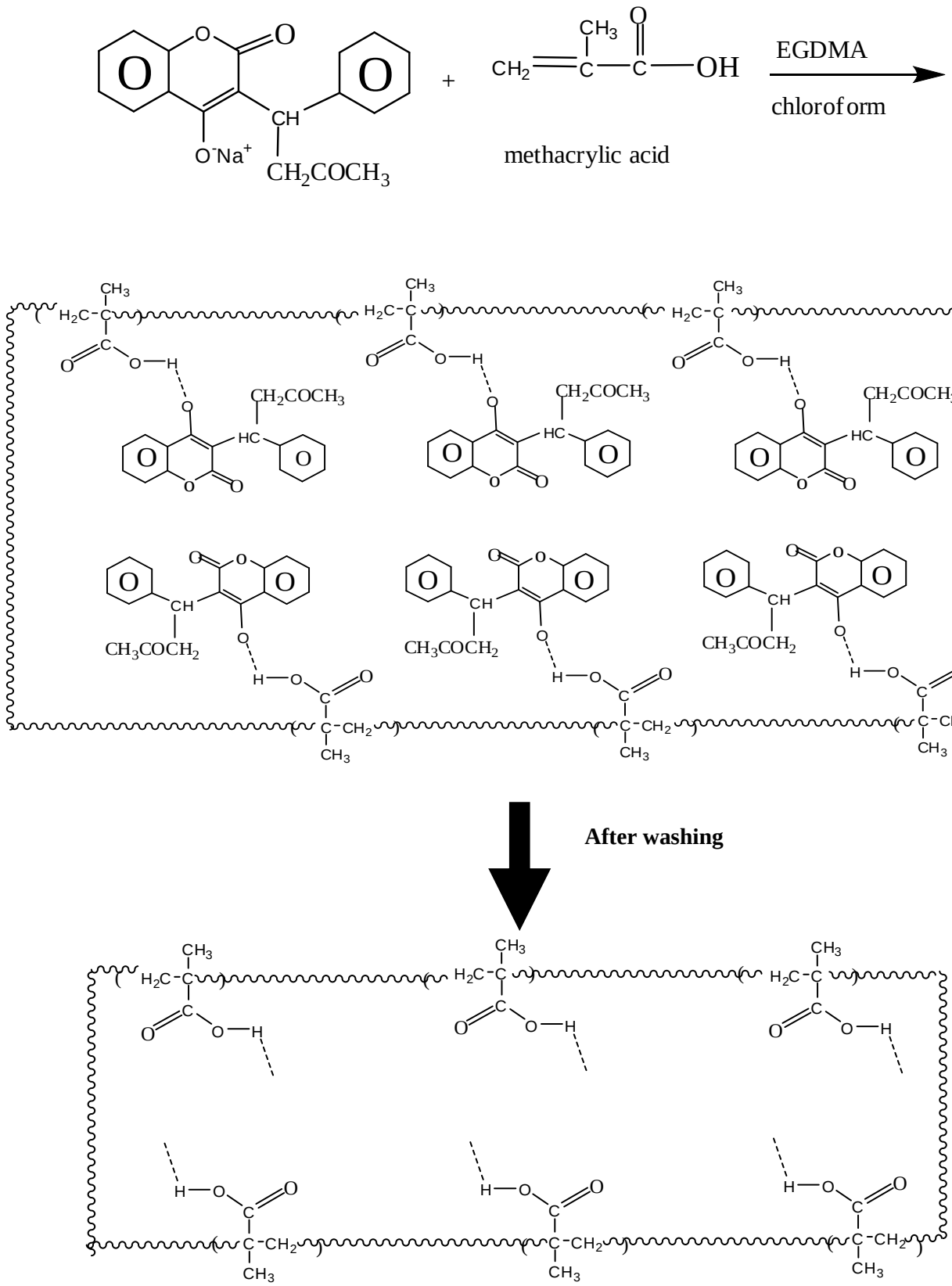
* Each measurement was repeated three times.

3.9 Synthesis of MIPs for Warfarin sodium (WFN):

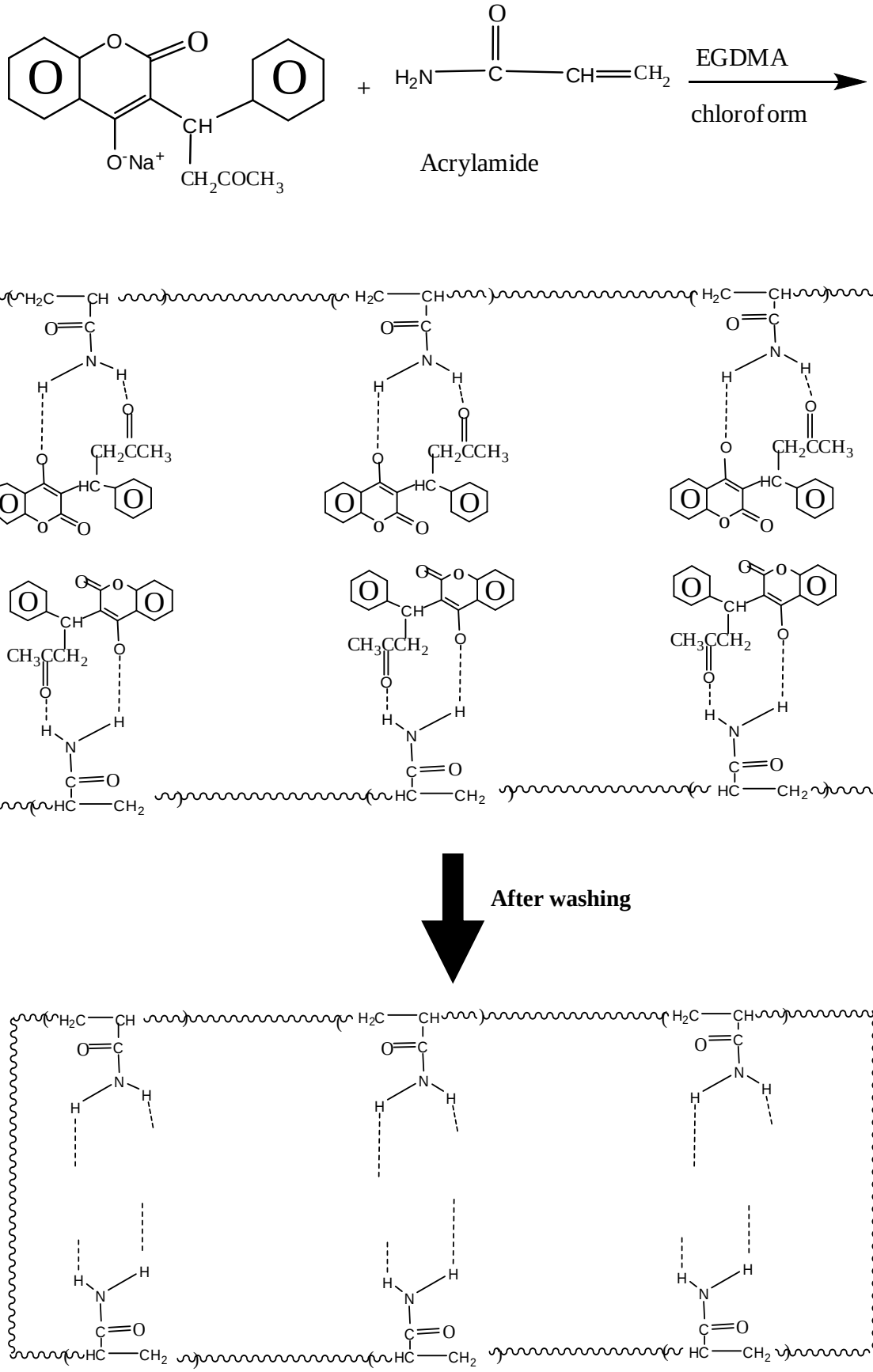
Four MIPs for (WFN) were synthesized by self-assembling (non-covalent) bulk polymerization method. The careful choice of functional monomer plays an important role to provide complementary interactions with the template .Two monomers, methacrylic acid (MAA) and acryl amide (ACY) were properly and effectively used for the synthesis of molecularly imprinted polymers (MIPs) and non- imprinted polymer (NIPs) although the acid-base properties of the two monomers are different. The carboxyl group on (MAA) and the amide group on Acrylamid are excellent hydrogen bond donor and acceptor. The kind and the amount of the cross-linking agent is another important choice as it controls the chemical environment and morphology of the polymer matrix and imparts mechanical stability to it. Ethylene glycol dimethacrylate (EGDMA) was used as a cross-linker that has acrylate groups that enable it to form more rigid polymer which lead to MIP with higher capacities and selectivity. In addition the method of polymerization restricts the type of solvent used. For bulk polymerization aprotic and a polar organic solvent were exclusively used mainly with low dielectric constant.The porogen is strongly influence the stability of the functional monomer-template complexes in the prepolymerization step. Over several solvents that were tested including dichloromethane, chloroform, DMSO; chloroform was found to be a suitable porogenic solvent.The suggested schemes (3.49),(3.50) and (3.51)illustrate the synthesis of MIPs for (WFN) based on (MAA) and (ACY) as acidic and basic functional monomer.



Figure(3.49): WFN-MIP synthesis, using Methacrylic acid (MAA) as an acidic functional monomer.



Figure(3.50): WFN-MIP synthesis, using Methacrylic acid (MAA) as an acidic functional monomer.



Figure(3.51): WFN-MIP synthesis, using Acrylamide (ACY) as an Basic functional monomer.

Several trails were performed using different ratios of (D:M:C)to find out the optimal ratio for the preparation of MIPs (WFN) . Among these trails the molar ratios (D:M:C) of (1:6:30) for WFN-MIPs has produced polymer with very suitable performance characteristics. These ratios are in consistence with some prepared MIPs found in literature. Tables (3.64) summarize the optimum ratios used in the synthesis of MIPs and NIPs for (WFN) drug.

Table (3.64): The different ratios of [D:M:C] and progens used in the synthesis of MIPs and NIPs for (WFN) .

	Drug WFN	Monomer MAA	Crosslinker EGDMA	Initiator	Solvent	Result
MIP1	**1** **0.500 mmole**	**2** **1.00 mmole**	**2** **1.00 mmole**	**0.1** **0.200 mmole**	**5 mL $CHCl_3$**	**Pile yellow Gel**
MIP2	**1** **0.500 mmole**	**3** **1.500 mmole**	**6** **3.00 mmole**	**0.3** **0.15 mmole**	**5 mL $CHCl_3$**	**Pile yellow Gel**
MIP3	**1** **0.500 mmole**	**4** **2.00 mmole**	**12** **6.00 mmole**	**0.4** **0.200 mmole**	**5 mL $CHCl_3$**	**Pile yellow not rigid**
MIP4	**1** **0.500 mmole**	**6** **3.00 mmole**	**30** **15.00 mmole**	**0.6** **0.300 mmole**	**5 mL $CHCl_3$**	**Pile yellow rigid**
NIP4		**6** **3.00 mmole**	**30** **15.00 mmole**	**0.6** **0.300 mmole**	**5 mL $CHCl_3$**	**White rigid**
	Drug WFN	**Monomer ACY**	**Crosslinker EGDMA**	**Initiator**	**Solvent**	**Result**
MIP1	**1** **0.500 mmole**	**6** **3.00 mmole**	**30** **15.00 mmole**	**0.6** **0.300 mmole**	**5 mL $CHCl_3$**	**Pile yellow rigid**
NIP 1		**6** **3.00 mmole**	**30** **15.00 mmole**	**0.6** **0.300 mmole**	**5 mL $CHCl_3$**	**White rigid**

All ratio prepared in water bath at 60 C^0 .

Other ratios with low percentage of cross-linker to functional monomer (less than 80%) results in a gel-like polymers of limited applications in MIPs. The presence of large excess of cross-linking agent produces a polymer with macro reticular networks, mechanically robust with a

permanent porous structure and high surface area. The final MIP was rigid enough to leave after the removal of template molecule specific recognition sites (cavities) with high affinity to the template molecules.

3.10 . Physical Characterization of Drug-MIPs

3.10.1. Spectroscopic Techniques

Infrared spectroscopy, in particular FTIR, is an important technique for polymer characterization and is broadly applied to the analysis of imprinted materials. It is very sensitive towards structural features such as functional groups incorporated into the material (carbonyl, aromatics...) of copolymer composition.

3.10.1.1. FTIR of Basic MIPs of (WFN).

The FTIR spectra of the drug , MIP based on (ACY) as basic functional monomer (before and after the removal of template) are shown in Figures (3.52),(3.53) and (3.54). Table (3.65) summarized the main peaks that appeared in these Figures.

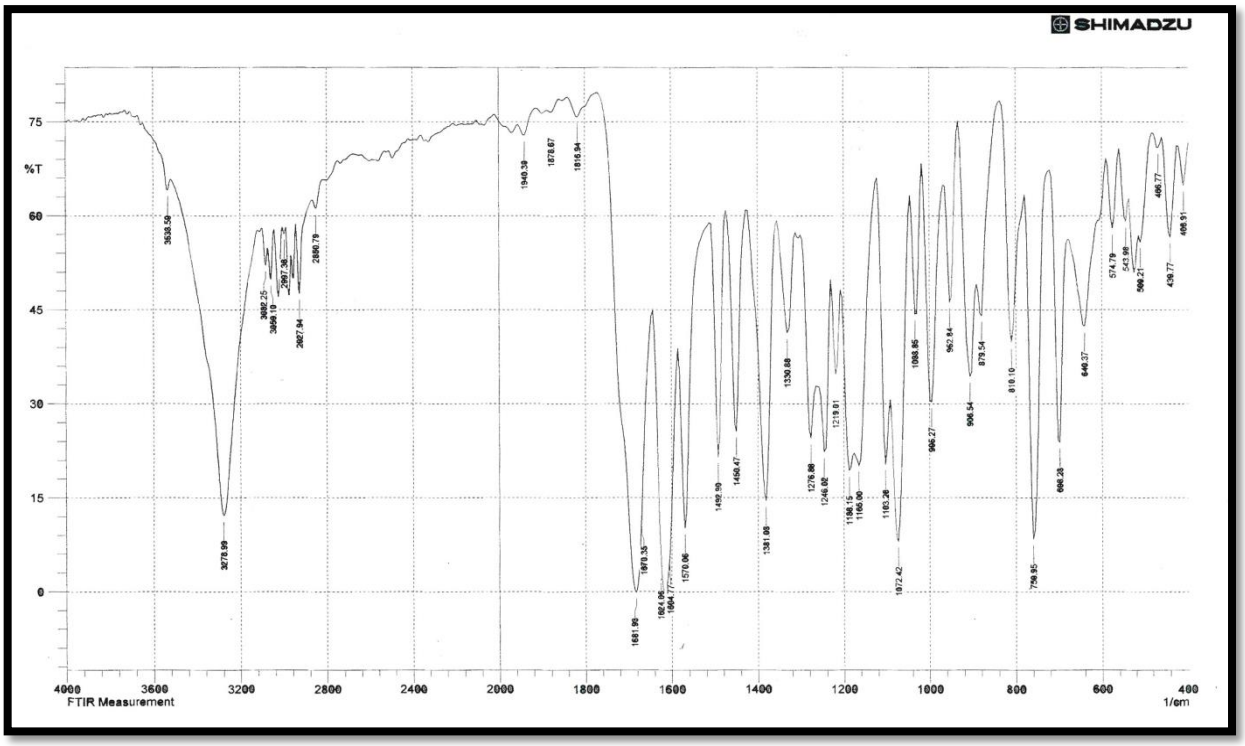


Figure (3.52): FTIR spectrum of standard warfarin sodium.

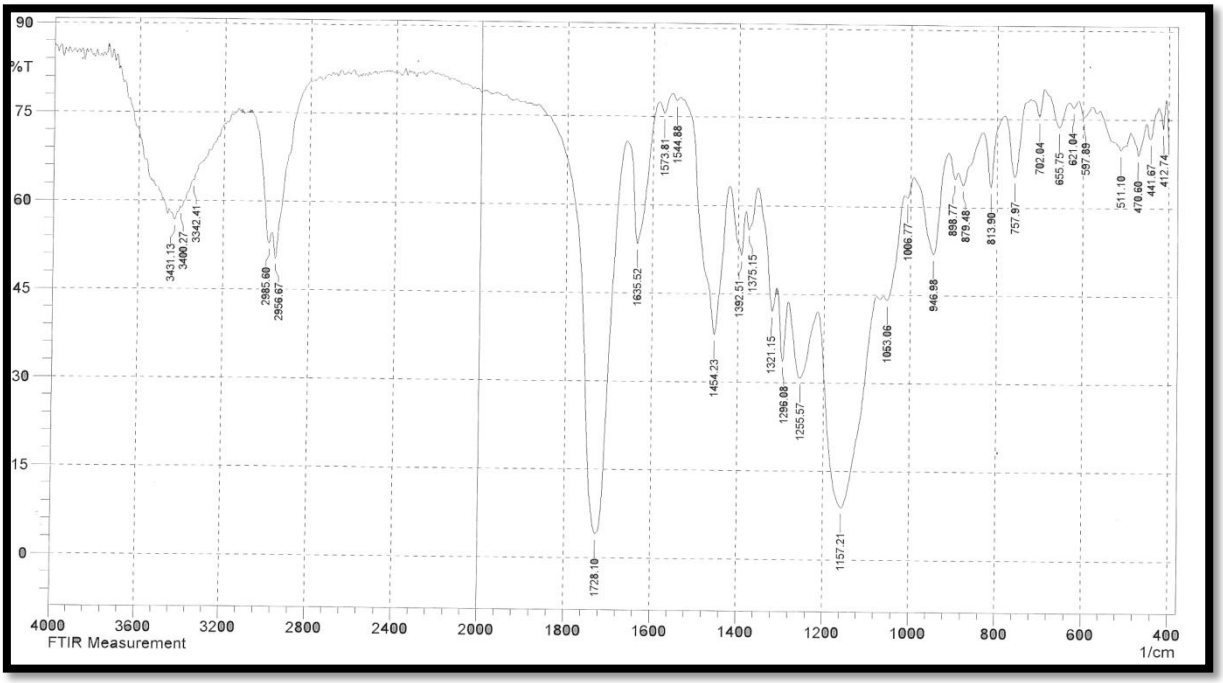


Figure (3.53): FTIR of WFN-MIP(ACY) before the removal of (WFN).

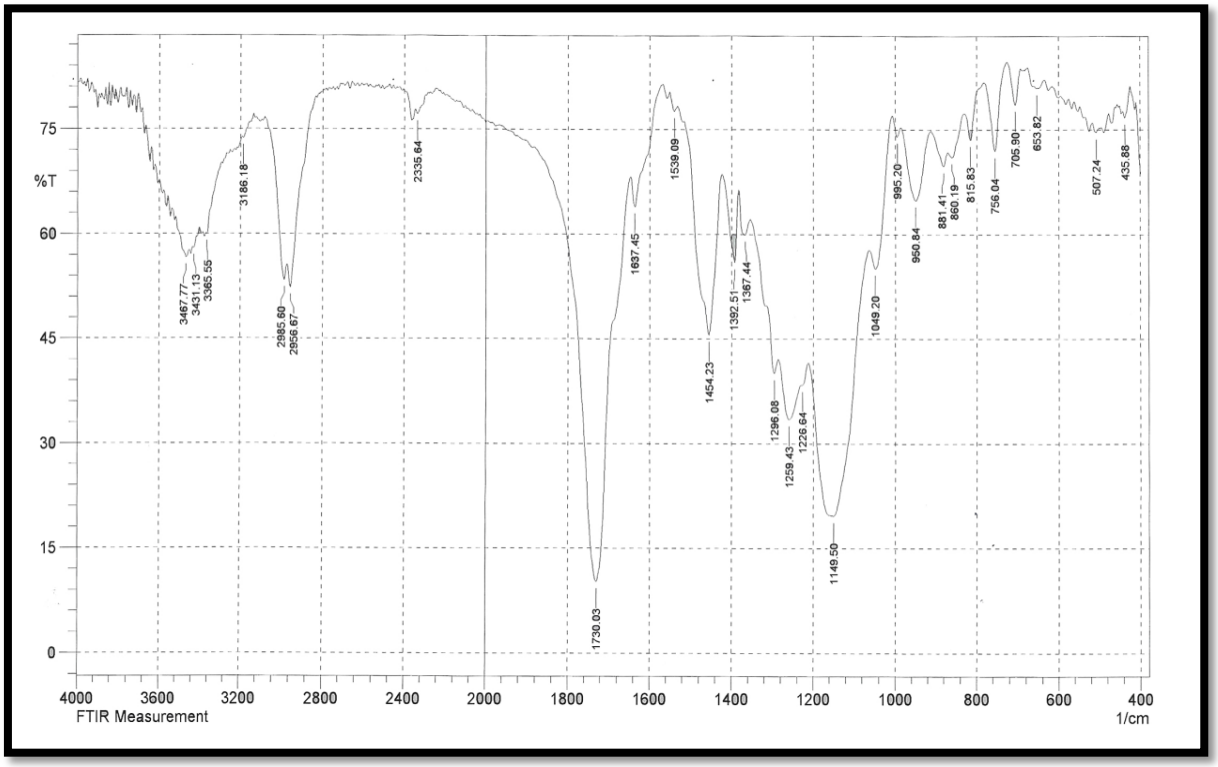


Figure (3.54): FTIR of WFN-MIP(ACY) after the removal of (WFN).

Table (3.65): The most identified peaks of FTIR spectra for WFN and WFN-MIP(ACY) befor and after removal of WFN using (ACY) as a functional monomer.

No.	Functional Group	WFN	WFN-MIP(ACY)before template removal	WFN-MIP(ACY)after template removal
1.	NH_2 str. asymm	---	3431	3467
2.	NH_2 str. symm	----	3400	3431
3.	OH str.	3278	----	----
4.	CH str. aromatic	3082	----	----
5.	CH str. alphatic	2927-2850	2985-2956	2985-2956
6.	C=O str. amide	----	1728	1730
7.	C=O str.ester	1681	----	----
8.	C=O str. keton	1670	----	----
9.	C=C str.	1604	1635	----
10.	C-O str. asymm	1246	1255	1259
11.	C-O str. symm	1188	1157	1149
12.	Out-of plane-mono-sub	759-698	----	----

From the Figure (3.52) FTIR spectrum for the drug (WFN) we can see the appearance of hydroxyl group stretching at (3278) cm^{-1} the Figure also show bands at (1681-1670) cm^{-1} that could be attributed to carbonyl groups stretching of ester and keton respectively ,and the Figure show bands at (759-698)cm^{-1} for the out of plane bending of mono substituted benzene ring.

From the Figure (3.53)FTIR spectrum for the WFN-MIP(ACY) before the removal of (WFN) show the following absorption : two bands at (3431 and 3400) cm^{-1} for (NH_2) groups asymmetrical and symmetrical.The CH aliphatic stretching appearance at (2985-2956)cm^{-1} and the carbonyl stretching of amid (1728) cm^{-1}, the band at (1635)cm^{-1} stretching for ($c_{=}c$) group.

From the figure (3.54) IR spectrum for the WFN-MIP(ACY) after the removal of (WFN) show the following absorption : two bands at (3467and 3431) cm^{-1} for (NH_2) groups asymmetrical and symmetrical. The CH aliphatic stretching appearance at (2985 and 2956)cm^{-1} and the carbonyl stretching of amid (1730) cm^{-1}, the band of ($c_{=}c$) group disappearance and shifiting the band with appearance at (1259and 1149)cm^{-1} of (c-o) groups asymmetrical and symmetrical.

On the other hand the control NIPs and MIPs after the removal of template have the similar spectra indicating the similarity in the backbone structure and prove that washing the MIP particles with 70% acetic acid solution used a Soxhlet extraction system is an efficient way to remove the template molecule leaving specific recognition binding sites in the polymer structure.

3.10.1.2. FTIR of Acidic MIP of (WFN).

The FTIR spectra of the MIP based on (MAA) as acidic functional monomer (before and after the removal of template) are shown in Figures (3.55) and (3.56). Table (3. 66) summarized the main peaks that appeared in these Figures.

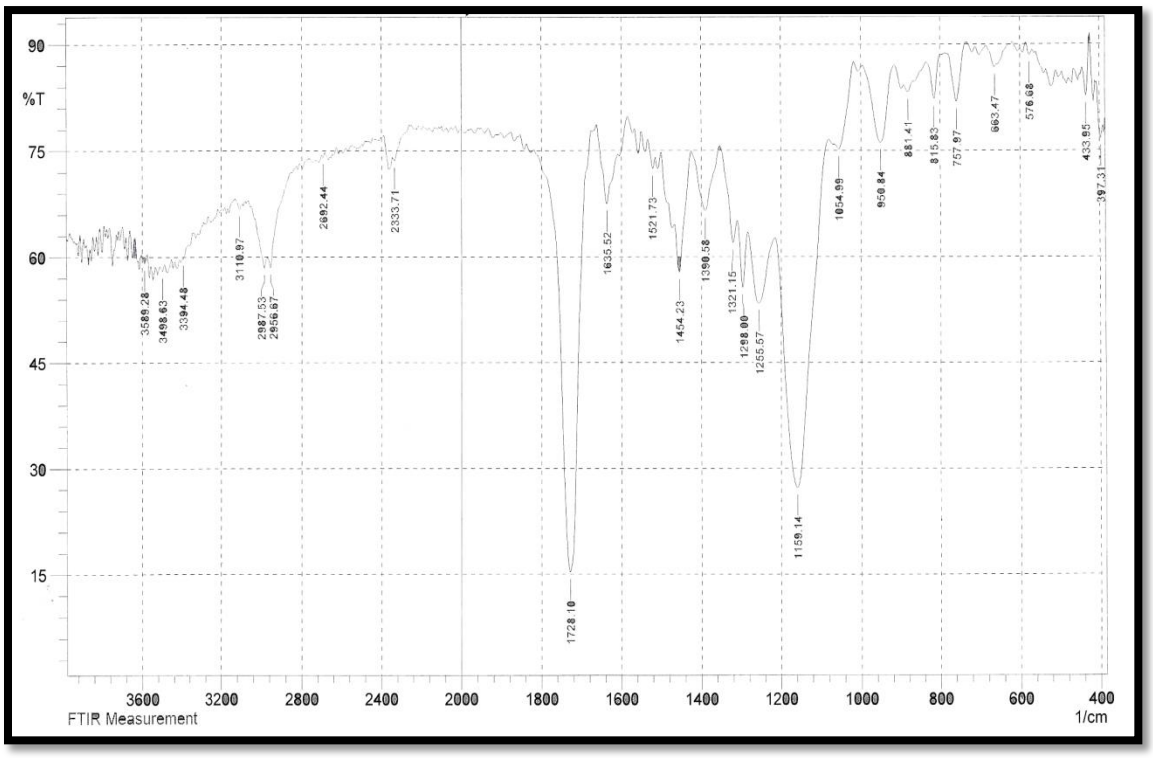


Figure (3.55): FTIR of WFN-MIP(MAA) before the removal of (WFN).

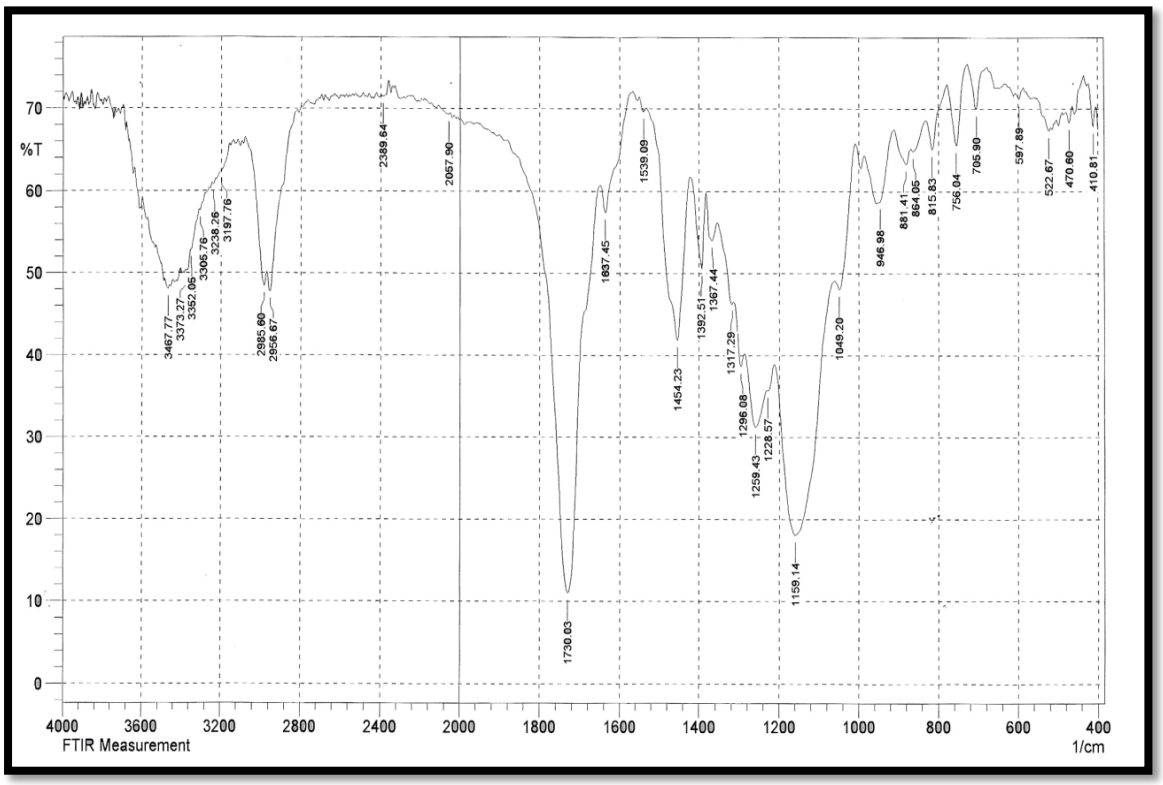


Figure (3.56): FTIR of WFN-MIP(MAA) after the removal of (WFN).

Table (3.66): The most identified peaks of FTIR spectra for WFN and WFN-MIP befor and after removal of WFN using (MAA) as a functional monomer.

No.	Functional Group	WFN	WFN-MIP(MAA)before template removal	WFN-MIP(MAA)after template removal
1.	OH str.	3278	3433	3431
2.	CH str. alphatic	2927-2850	2987-2848	2991-2894
3.	C=O str.ester	1681	----	----
4.	C=O str.acid	----	1728	1728
5.	C=O str.keton	1670	----	----
6.	C=C str.	1624	1635	----
7.	C-H bending	1450-1381	1454-1392	1454-1388
8.	C-O str. asymm.	1246	1259	1259
9.	C-O str. symm.	1188	1159	1159
10.	Out-of plane-mono-sub	759-698	----	----

The Figure (3.55) FTIR spectrum of WFN-MIP(MAA) before the removal of (WFN) show appearance band at (1728) cm^{-1} for carbonyl group of acid stretching ,also show band for (c=c) group stretching at (1635) cm^{-1} and (C-H) group bending at (1454 and 1392) cm^{-1} ,(c-o) group stretching asymmetrical and symmetrical at (1259 and 1159) cm^{-1}.

The Figure (3.56) FTIR spectrum of WFN-MIP(MAA) after the removal of (WFN) show the following :the carbonyl group of stretching acid at (1728) cm^{-1} acid and disappearance the (c=c) group stretching also the carbonyl group of stretching ester and keton disappearance, the (C-H)

bending group appearance at (1454 and 1388) cm^{-1} and (c-o) stretching asymmetrical and symmetrical show bands at (1259 and 1159) cm^{-1} respectively.

On the other hand the control NIPs and MIPs after the removal of template have the similar spectra indicating the similarity in the backbone structure and prove that washing the MIP particles with 30% acitic acid solution is an efficient way to remove the template molecule leaving specific recognition binding sites in the polymer structure.

3.11.Morphological Characterization:

The technology of molecular imprinting allows for the preparation of synthetic polymers with specific binding sites for a target molecule. This can be achieved if the target is present during the polymerization process, thus acting as a molecular template. Monomers carrying certain functional groups are arranged around the template through either noncovalent or covalent interactions. Following polymerization with a high degree of cross-linking, the functional groups are held in position by the polymer network. Subsequent removal of the template by solvent extraction or chemical cleavage leaves cavities that are complementary to the template in terms of size, shape and arrangement of functional groups. These highly specific receptor sites are capable of rebinding the target molecule with a high specificity, sometimes comparable to that of antibodies. Molecularly imprinted polymers have therefore been dubbed "antibody mimics". It has been shown that they can be substituted for biological receptors in certain formats of immunoassays and biosensors. They have also been used as stationary phases for affinity separations, for the screening of combinatorial libraries, and as enzyme mimics in catalytic applications.

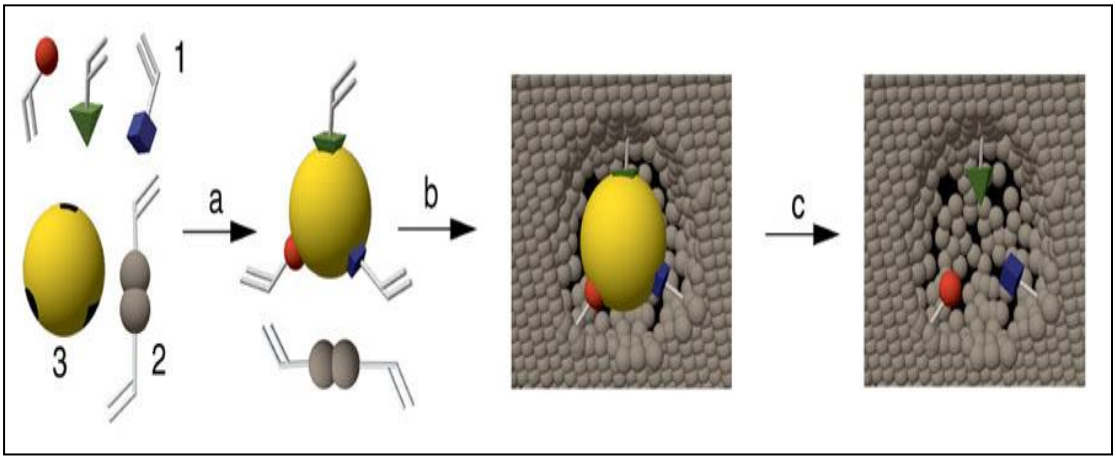


Figure (3.57) : The steps of Molecularly Imprinted Polymer preparation.

Scanning electron microscopy (SEM) was used for primary evaluation of the MIP particles, obtained by different methods. Figures (3.58) and (3.59) show the SEM images of the obtained polymers. It can be seen that the views of the polymer particles are different considerably, depending on the method of the MIP preparation. Microemulsion polymerization gives very small particles. Spherically shaped polymeric particles with small sizes around 5-20 μm can be distinguished in the related image.

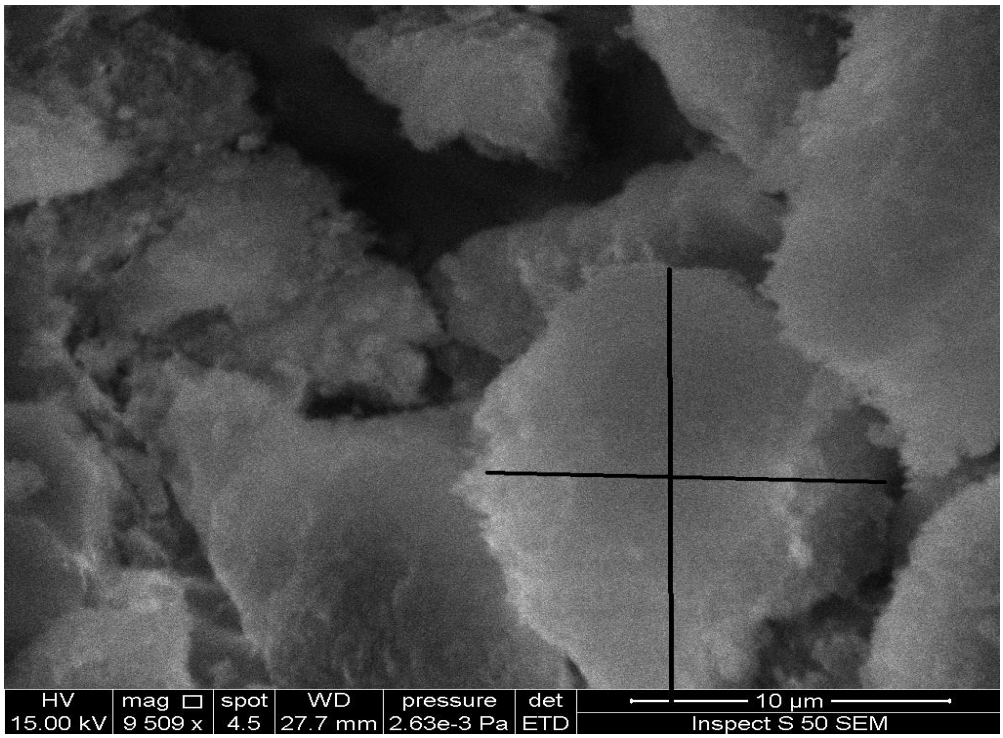


Figure (3.58): Scanning electron micrographs of [WFN-MIP(ACY)]obtained by bulk polymerization

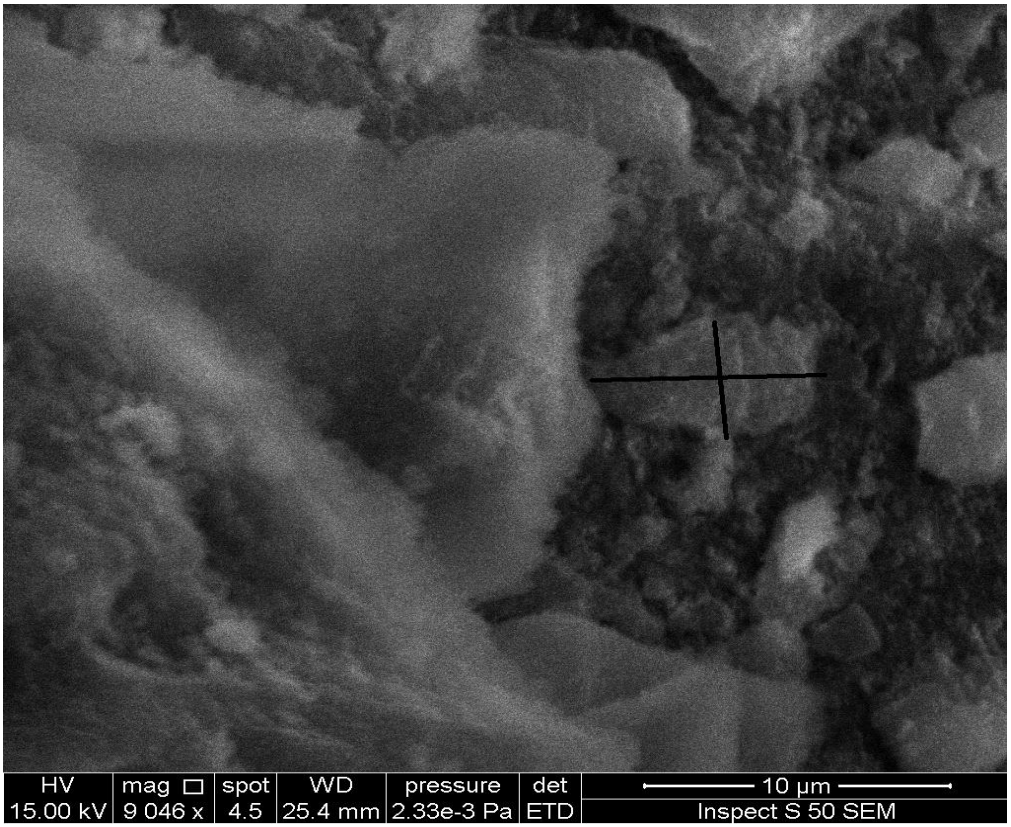


Figure (3.59): Scanning electron micrographs of [WFN-MIP(MAA)]obtained by bulk polymerization

3.12.Characterization of MIP electrodes for WFN:

MIP based ion selective electrodes (ISE) for the determination of (WFN) were fabricated. The electrodes based on WFN-MIPs using (MAA) and (ACY) as functional monomers incorporated in PVC matrix and plasticized with (TP and DBS) plasticizers. Their Nernsation response and working range were investigated. The thickness of the membrane highly affects its characteristics.This was indicated by the excellent response and dynamic working range attained when membrane thickness was about 1mm.The specifications of MIP ion selective electrode for (WFN) are summarized in Table (3.67).

Table (3.67): The characteristics of the WFN-MIP ISE based on different functional monomers and plasticizers.

Electrode no.	I	II	III	IV
Type of Electrode	**WFN- MIP(ACY)+ EGDMA + TP**	**WFN- MIP(ACY) + EGDMA +DBS**	**WFN- MIP(MAA)+ EGDMA+TP**	**WFN- MIP(MAA)+ EGDMA+DBS**
***Slope mV/decade**	57.13	52.34	58.41	51.80
Detection limit (M)	4×10^{-6}	3×10^{-5}	2.5×10^{-6}	3.5×10^{-5}
Correlation coefficient	0.9987	0.9996	0.9994	0.9996
Linear range(M)	1×10^{-5}-1×10^{-1}	1×10^{-4}-1×10^{-1}	1×10^{-5}-1×10^{-1}	1×10^{-4}-1×10^{-1}
Life time(day)	~45	~30	~30	~22

As it can be seen that electrodes (I and III) exhibited a near- Nernsation response represented by a slope of 57.13, 58.41 mV/decade respectively with linear dynamic concentration range (1×10^{-5}-1×10^{-1})M and lower detection limit ($4\times10^{-6}-2.5\times10^{-6}$) M.

3.13.Effect of Plasticizer

The plasticizer to be used in membrane should exhibit high lipophilicity, have high molecular weight, low tendency for exudation from the polymer matrix, low vapor pressure and high capacity to dissolve the substrate and other additives present in the membrane. Moreover, its viscosity and dielectric constant should be adequate. The nature of a plasticizer or membrane solvent greatly affects all the electrochemical characteristics including potentiometric selectivity because it influences both the dielectric constant of the membrane and the mobility of the molecule or ion within the membrane. Therefore, four

membrane compositions were investigated by using two type of plasticizer (TP and DBS) as shown in Figures (3.60) and (3.61).

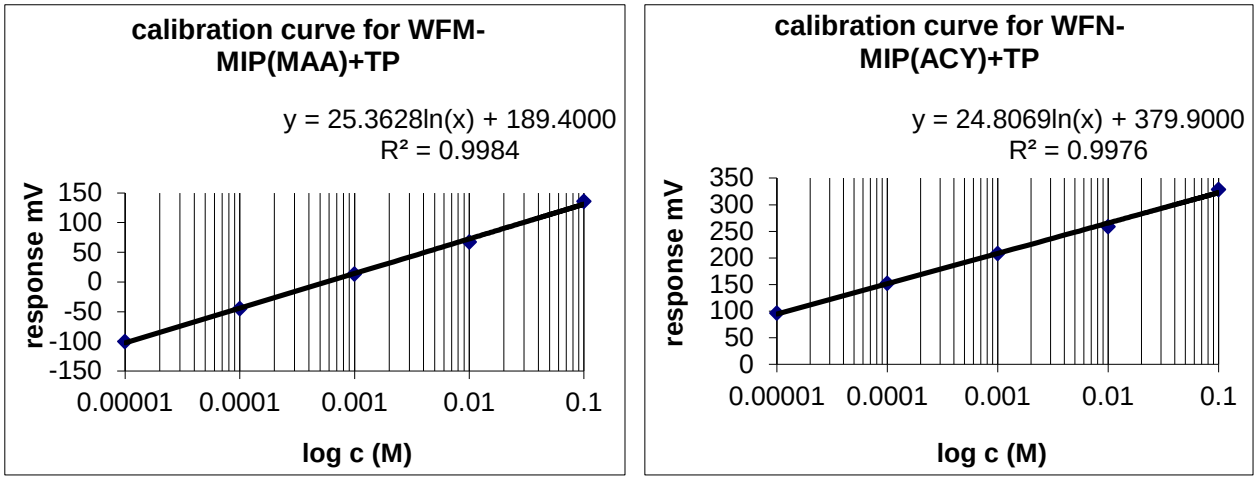


Figure (3.60) Calibration curve for WFN-MIP(ACY),(MAA) by using TP as plasticizer.

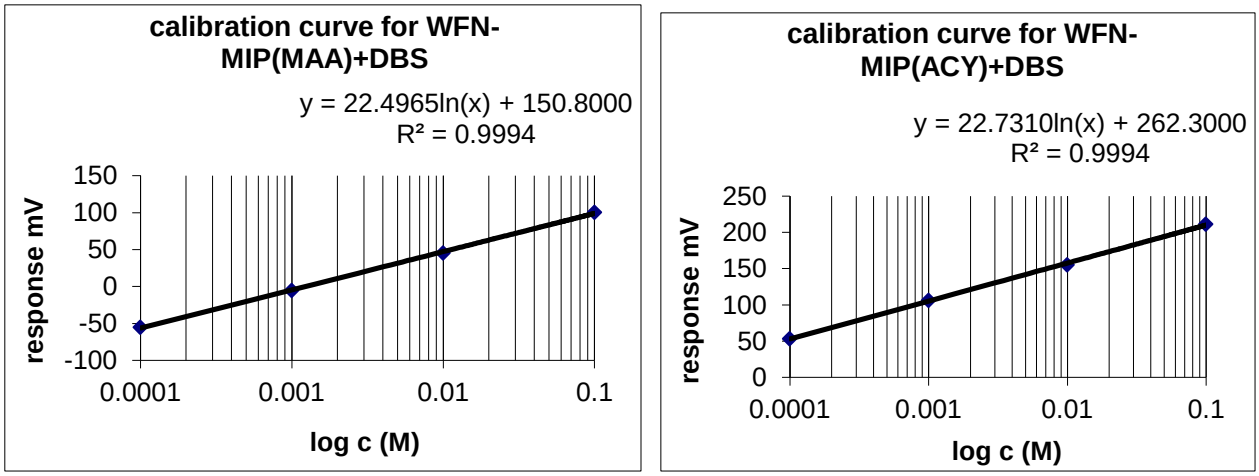


Figure (3.61) Calibration curve for WFN-MIP(ACY),(MAA) by using DBS as plasticizer.

The results shown in table (3.67) for electrodes (I and III) indicate that membrane plasticized with (TP) displayed better performance Attributed to be more compatible with the WFN-MIP as it produces a homogenous and clear membrane having better slope and longer life time. This may be due to that plasticizers have a good fusion rate and viscosity that lead to higher diffusivity in the prepared membrane and therefore imparting a better response to the sensor. Figure (3.62) shows the structure of TP plasticizer.

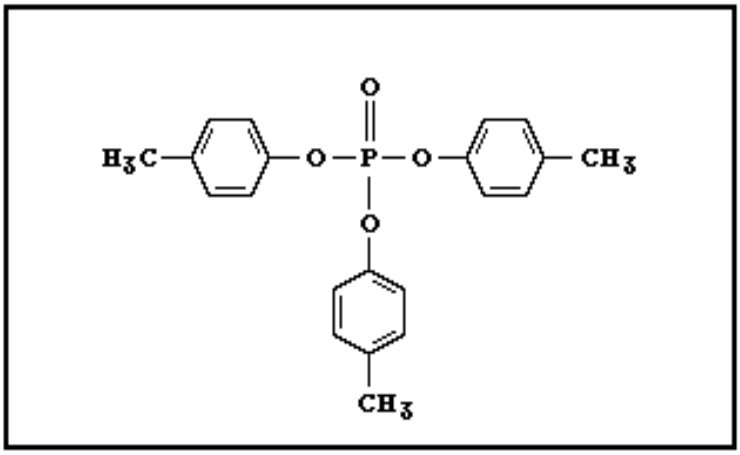
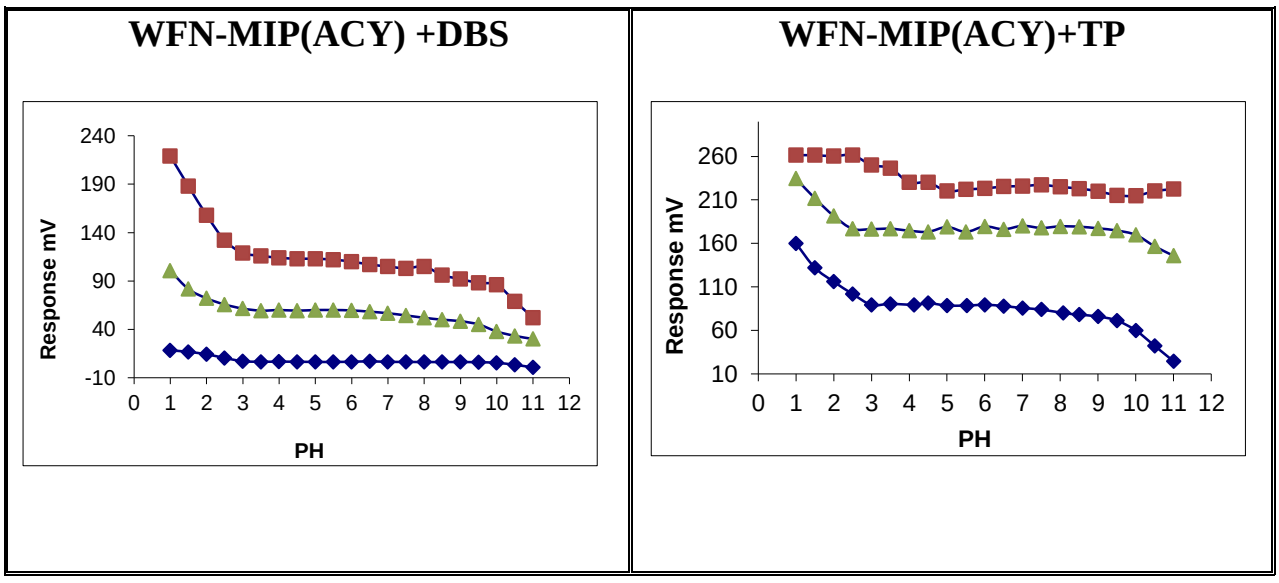


Figure (3.62): Structure of TP plasticizer.

3.14.Effect of pH :

The effect of pH on the potential readings of the electrodes (I,II,III and IV) was studied by immersing a combined glass electrode, (WFN) ISE and a saturated calomel reference electrode in 50 ml beakers containing 25 ml aliquots of 1.0×10^{-2} 1.0×10^{-3} and 1.0×10^{-4} M of (WFN) aqueous solutions. The pH of each solution was adjusted by 0.1M Ammonium hydroxide or hydrochloric acid solutions. The potential reading at each pH value was recorded. A plot of pH values versus the potential of the electrode is illustrated in Figure (3.63).



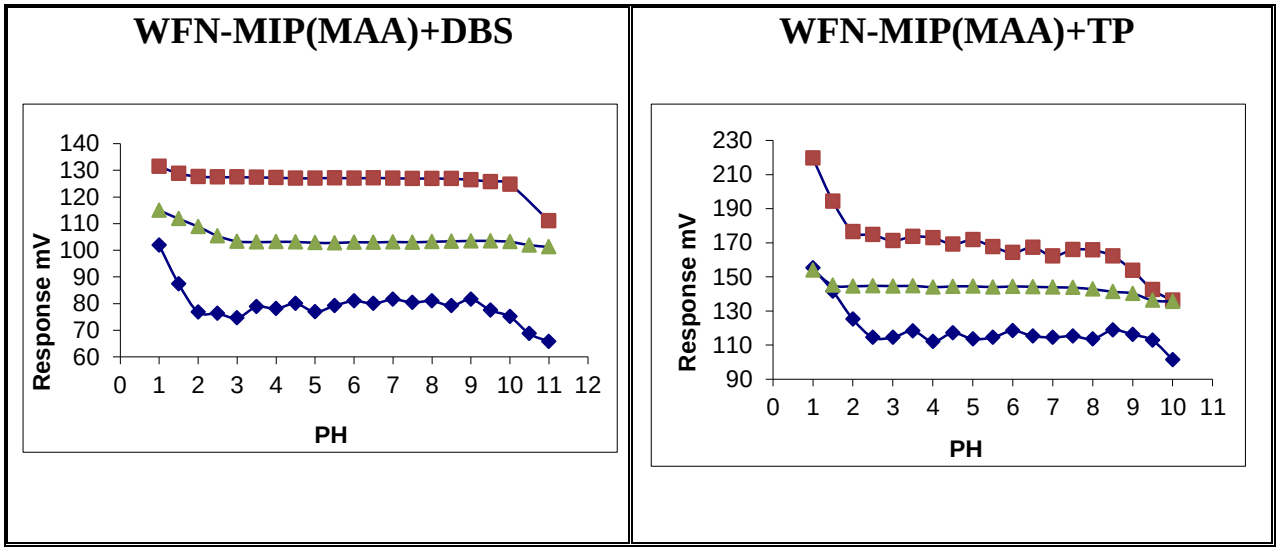


Figure (3.63): Effect of pH on the potential of the warfarin sodium MIPs electrodes at concentrations (■10^{-2}, ▲ 10^{-3} and ■ 10^{-4}) M.

3.15.The Selectivity Study:

The influence of the interfering ions on the response behavior of ion selective membrane electrode is usually described in terms of selectivity coefficients. The selectivity coefficients for WFN (K^{pot}) over a wide range of interfering molecules, mono-valente , di-valent and Tri-valent ions were determined by the separate solutions method (SSM) . The selectivity coefficients calculated for WFN over each interference at aA= aB in a series of concentrations ranged (1.0×10^{-6}-1.0×10^{-1}) M for each of the two separate solutions, i.e. the WFN solutions and the interference solutions, were below the unity which indicate that these species do not interfere in the determination of WFN.

3.15.1. Selectivity measurement by separation method (SSM):

The selectivity of WFN electrodes was measured by separated solution method for concentrations range (10^{-6} – 10^{-1}) M of WFN solutions. The concentrations for different (K^{+}, Ca^{2+}, Al^{3+},Alanine ,Proline and Serine) was ranged from (10^{-1} to 10^{-6}) M and the potentiometric selective coefficients were calculated by using equation (1-8). The values of $K_{A,B}$ and potential of interference ions are listed in Tables (3. 68) to (3.71) and the selectivities toward the studied species are shown in Figure (3.64) and (3.65):

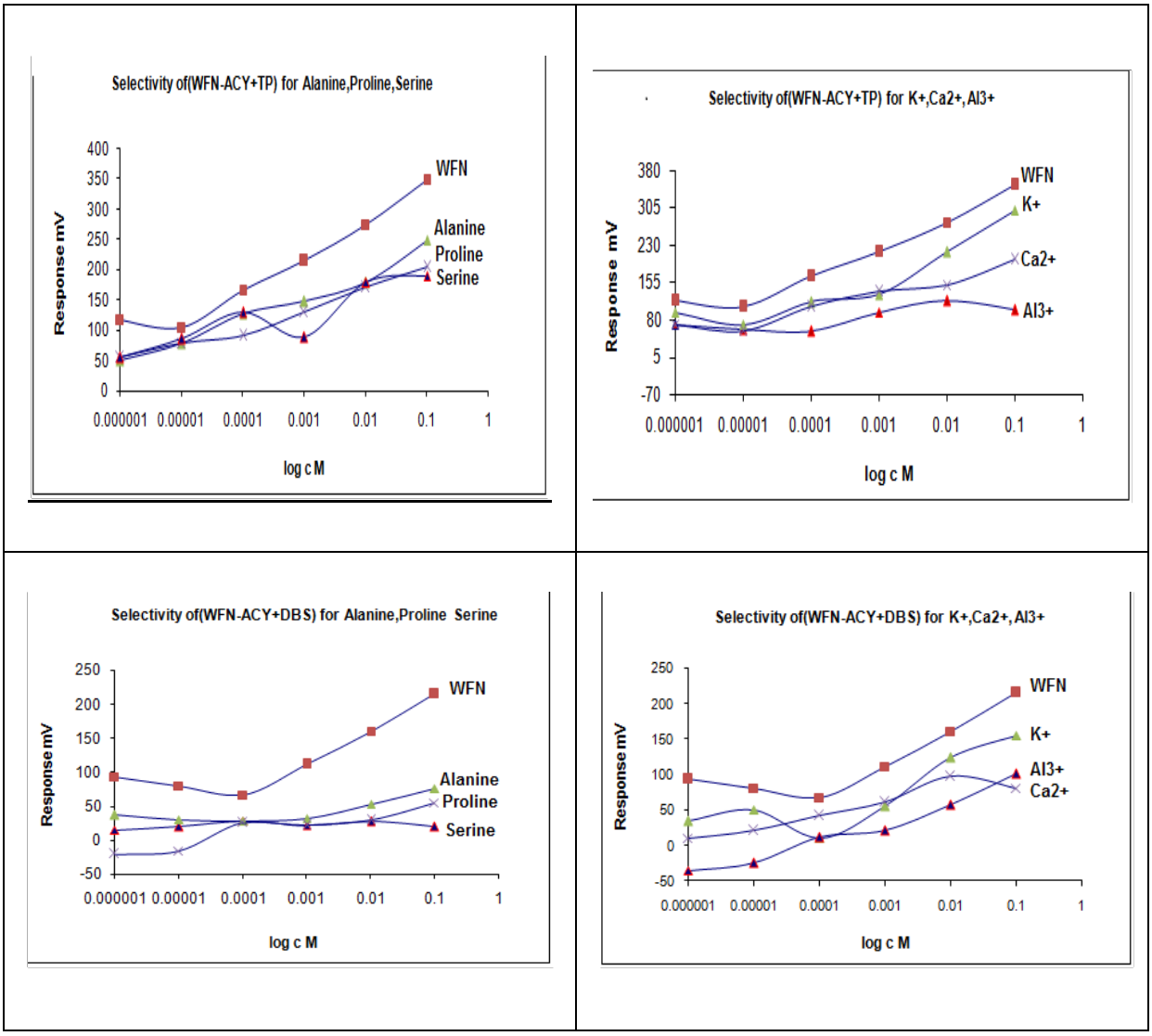
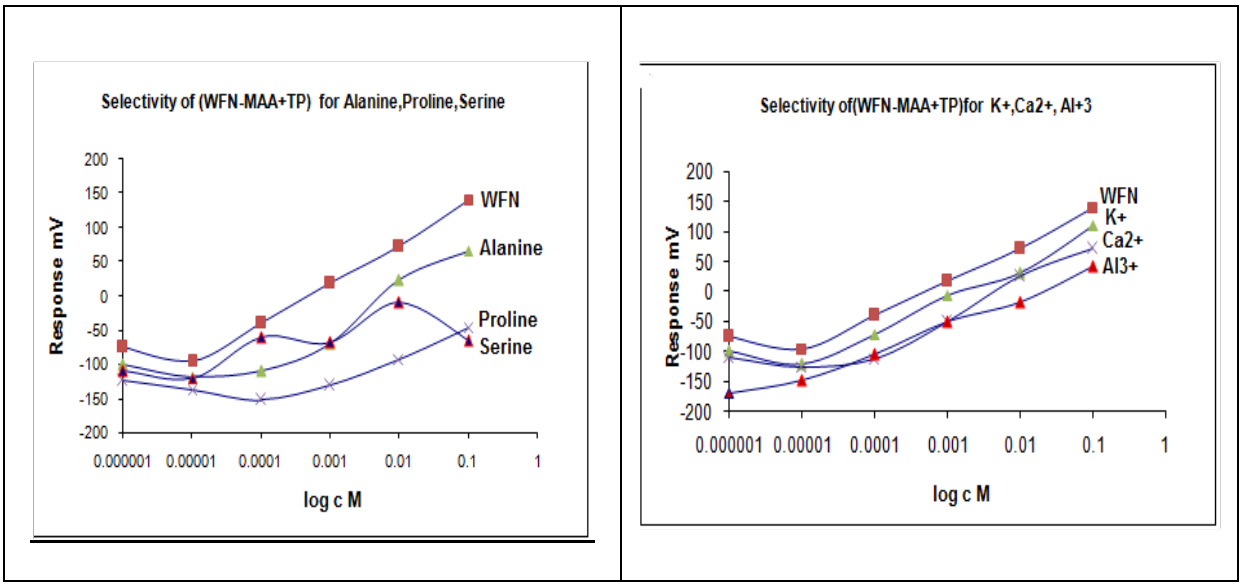


Figure (3.64): Selectivity of (WFN – MIP(ACY) and the interfering cations , amino acid by separation solution method, by using TP,DBS as a plasticizer.



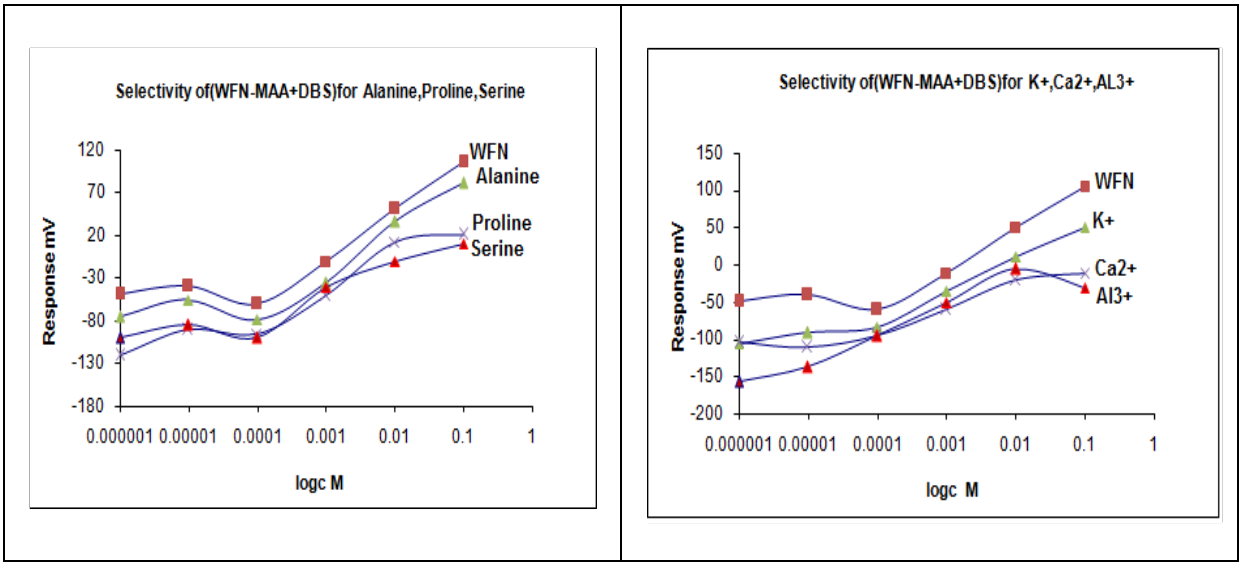


Figure (3.65): Selectivity of (WFN – MIP(MAA) and the interfering cations , amino acid by separation solution method, by using TP,DBS as a plasticizer.

selectivity coefficient of Molecularly imprinted polymer measurement by Separation solution method the result show good selectivity and not interference with inorganic ion and the value of K_{pot} less than one that meaning the electrodes response to drug more than ion .

Table (3.68): Selectivity Coefficients for WFN-MIP(ACY)+TP electrode at different concentrations by separation solution method.

Interfering ions	Concentrations of warfarin sodium (M)											
	10^{-1}		10^{-2}		10^{-3}		10^{-4}		10^{-5}		10^{-6}	
	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$
K^+	300.1	1.316×10^{-1}	215.6	9.016×10^{-2}	130.5	3.278×10^{-2}	115.3	1.229×10^{-1}	70.3	2.410×10^{-1}	95.3	3.957×10^{-1}
Ca^{2+}	200.1	7.398×10^{-4}	150.3	6.486×10^{-4}	135.6	1.273×10^{-3}	105.3	8.217×10^{-4}	56.3	4.335×10^{-4}	70.2	1.438×10^{-4}
Al^{3+}	99.5	8.734×10^{-6}	118.3	8.277×10^{-5}	95.3	7.916×10^{-5}	55.6	2.381×10^{-5}	60.4	7.478×10^{-5}	70.1	1.426×10^{-5}
Alanine	250.1	1.755×10^{-2}	179.8	2.129×10^{-2}	148.6	6.799×10^{-2}	127.3	1.994×10^{-1}	77.8	3.261×10^{-1}	50.4	6.478×10^{-2}
Proline	205.3	2.885×10^{-3}	170.5	1.464×10^{-2}	130.7	3.304×10^{-2}	92.3	4.866×10^{-2}	80.1	3.578×10^{-1}	55.6	7.989×10^{-2}
Serine	190.7	1.601×10^{-3}	180.4	2.182×10^{-2}	88.7	6.081×10^{-3}	130.7	2.287×10^{-1}	85.7	7.311×10^{-2}	55.6	7.989×10^{-2}

Table (3.69): Selectivity Coefficients for WFN-MIP(ACY)+DBS electrode at different concentrations by separation solution method.

Interfering ions	Concentrations of warfarin sodium (M)											
	10^{-1}		10^{-2}		10^{-3}		10^{-4}		10^{-5}		10^{-6}	
	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$
K^+	155.3	7.139×10^{-2}	123.4	1.937×10^{-1}	55.3	8.438×10^{-2}	10.3	8.146×10^{-2}	50.4	2.671×10^{-1}	33.6	7.139×10^{-2}
Ca^{2+}	80.6	8.441×10^{-4}	97.3	6.147×10^{-3}	60.7	3.383×10^{-3}	41.3	3.186×10^{-3}	20.3	2.247×10^{-4}	10.4	2.572×10^{-5}
Al^{3+}	100.3	1.367×10^{-3}	57.3	4.902×10^{-4}	20.3	1.805×10^{-4}	10.9	1.796×10^{-4}	-25.3	4.420×10^{-6}	-35.4	3.414×10^{-7}
Alanine	76.7	2.248×10^{-3}	53.4	8.911×10^{-3}	32.7	3.122×10^{-2}	28.9	1.846×10^{-1}	30.4	1.108×10^{-1}	37.3	8.401×10^{-2}
Proline	95.3	5.096×10^{-3}	48.6	7.214×10^{-3}	35.6	3.547×10^{-2}	15.4	1.019×10^{-1}	-15.4	1.477×10^{-2}	-20.5	6.607×10^{-3}
Serine	100.3	6.350×10^{-3}	45.3	6.240×10^{-3}	70.5	1.646×10^{-1}	45.6	3.849×10^{-1}	10.3	4.578×10^{-2}	-55.6	1.410×10^{-3}

Table (3.70): Selectivity Coefficients for WFN-MIP(MAA)+TP electrode at different concentrations by separation solution method.

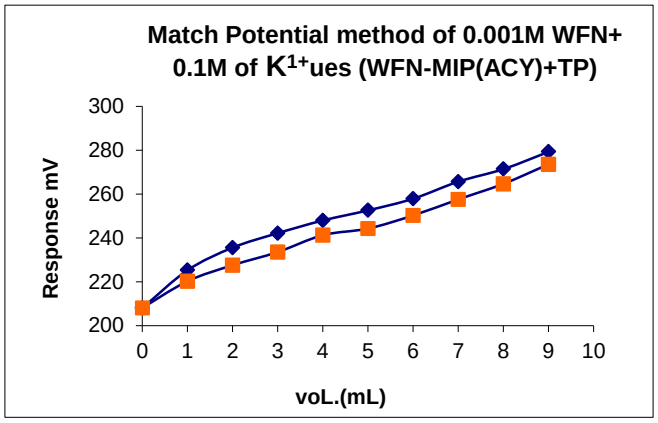
Interfering ions	Concentrations of warfarin sodium (M)											
	10^{-1}		10^{-2}		10^{-3}		10^{-4}		10^{-5}		10^{-6}	
	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$
K^+	110.8	3.101×10^{-1}	30.5	1.978×10^{-1}	-5.8	3.928×10^{-1}	-70.6	3.052×10^{-1}	-120.8	3.732×10^{-1}	-100.3	3.821×10^{-1}
Ca^{2+}	70.5	2.002×10^{-2}	25.6	1.631×10^{-2}	-50.3	2.149×10^{-3}	-111.4	6.111×10^{-4}	-125.6	9.768×10^{-4}	-108.5	2.766×10^{-4}
Al^{3+}	42.3	4.485×10^{-3}	-17.3	1.393×10^{-3}	-50.7	6.676×10^{-4}	-105.6	1.649×10^{-4}	-148.3	5.836×10^{-5}	-168.9	2.545×10^{-6}
Alanine	65.9	5.282×10^{-2}	22.3	1.432×10^{-1}	-70.6	3.053×10^{-2}	-110.1	6.282×10^{-2}	-118.3	4.119×10^{-1}	-101.1	3.703×10^{-1}
Proline	-45.7	6.489×10^{-4}	-92.5	1.550×10^{-3}	-130.7	2.857×10^{-3}	-152.7	1.176×10^{-2}	-137.3	1.947×10^{-1}	-125.1	1.437×10^{-1}
Serine	-65.8	2.938×10^{-4}	-10.5	3.930×10^{-2}	-68.9	3.265×10^{-2}	-60.7	4.509×10^{-1}	-120.8	3.732×10^{-1}	-110.5	2.556×10^{-1}

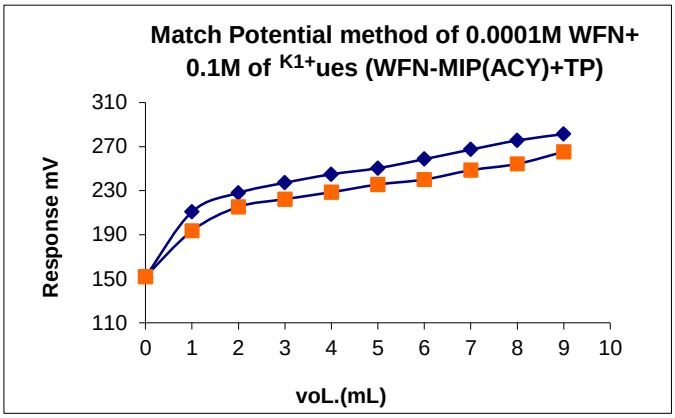
Table (3.71): Selectivity Coefficients for WFN-MIP(MAA)+DBS electrode at different concentrations by separation solution method.

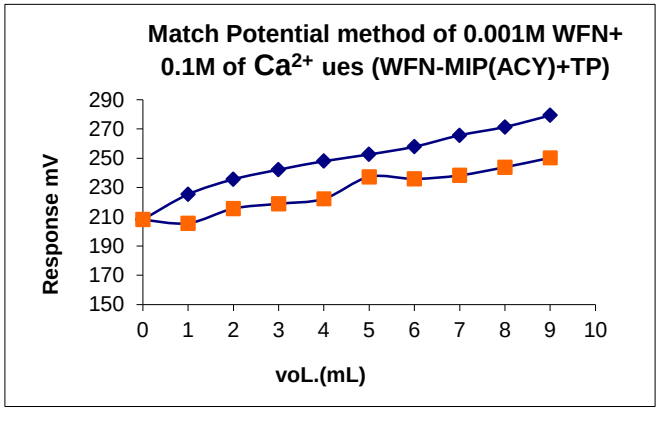
Interfering ions	Concentrations of warfarin sodium (M)											
	10^{-1}		10^{-2}		10^{-3}		10^{-4}		10^{-5}		10^{-6}	
	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$	$E_{B(mV)}$	$K_{A,B}$
K^+	50.7	8.790×10^{-2}	10.6	1.704×10^{-1}	-35.6	3.306×10^{-1}	-83.6	3.565×10^{-1}	-90.7	1.054×10^{-1}	-105.6	8.296×10^{-2}
Ca^{2+}	-10.7	1.814×10^{-3}	-20.7	4.240×10^{-3}	-60.7	3.425×10^{-3}	-95.7	2.082×10^{-3}	-110.7	1.371×10^{-4}	-105.3	8.408×10^{-5}
Al^{3+}	-30.7	5.076×10^{-4}	-5.7	3.828×10^{-3}	-50.7	1.685×10^{-3}	-95.7	4.472×10^{-4}	-137.6	6.064×10^{-6}	-157.8	8.113×10^{-7}
Alanine	80.7	3.335×10^{-1}	35.7	5.202×10^{-1}	-35.7	3.291×10^{-1}	-78.6	4.452×10^{-1}	-55.9	4.954×10^{-1}	-75.6	3.148×10^{-1}
Proline	20.1	2.255×10^{-2}	12.3	1.838×10^{-1}	-50.7	1.689×10^{-1}	-95.6	2.091×10^{-1}	-90.7	1.054×10^{-1}	-120.7	4.240×10^{-2}
Serine	10.4	1.465×10^{-2}	-10.7	6.613×10^{-2}	-40.8	2.623×10^{-1}	-100.3	1.697×10^{-1}	-85.3	1.340×10^{-1}	-99.6	1.083×10^{-1}

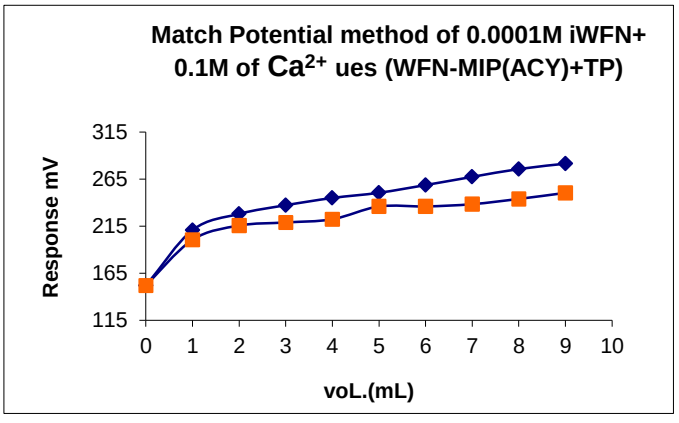
3.15.2. Selectivity measurement by Match potential method (MPM):

In this method the selectivity coefficient is given by using equation (1-6) is defined by the ratio of the activity of the primary ion relative to an interfering ion when they generate identical potentials in the same reference solution. In this method both monovalent ions are treated in the same manner, and the valence of the ions does not influence the selectivity coefficient. The results of selectivity coefficient are shown in Figure (3.66) to (3.73) and in the Table (3.72)and (3.73) were calculated from The concentration of the interfering ion which endued the same amount of the potential change as that induced by the increase of the concentration of primary ion.









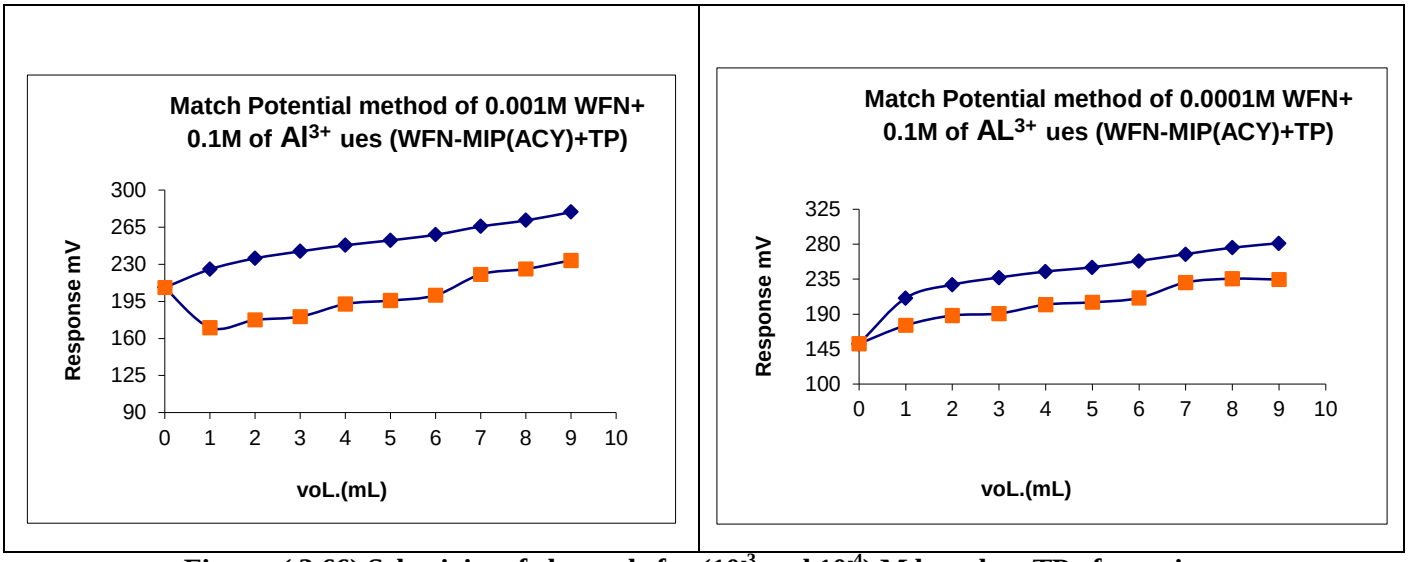
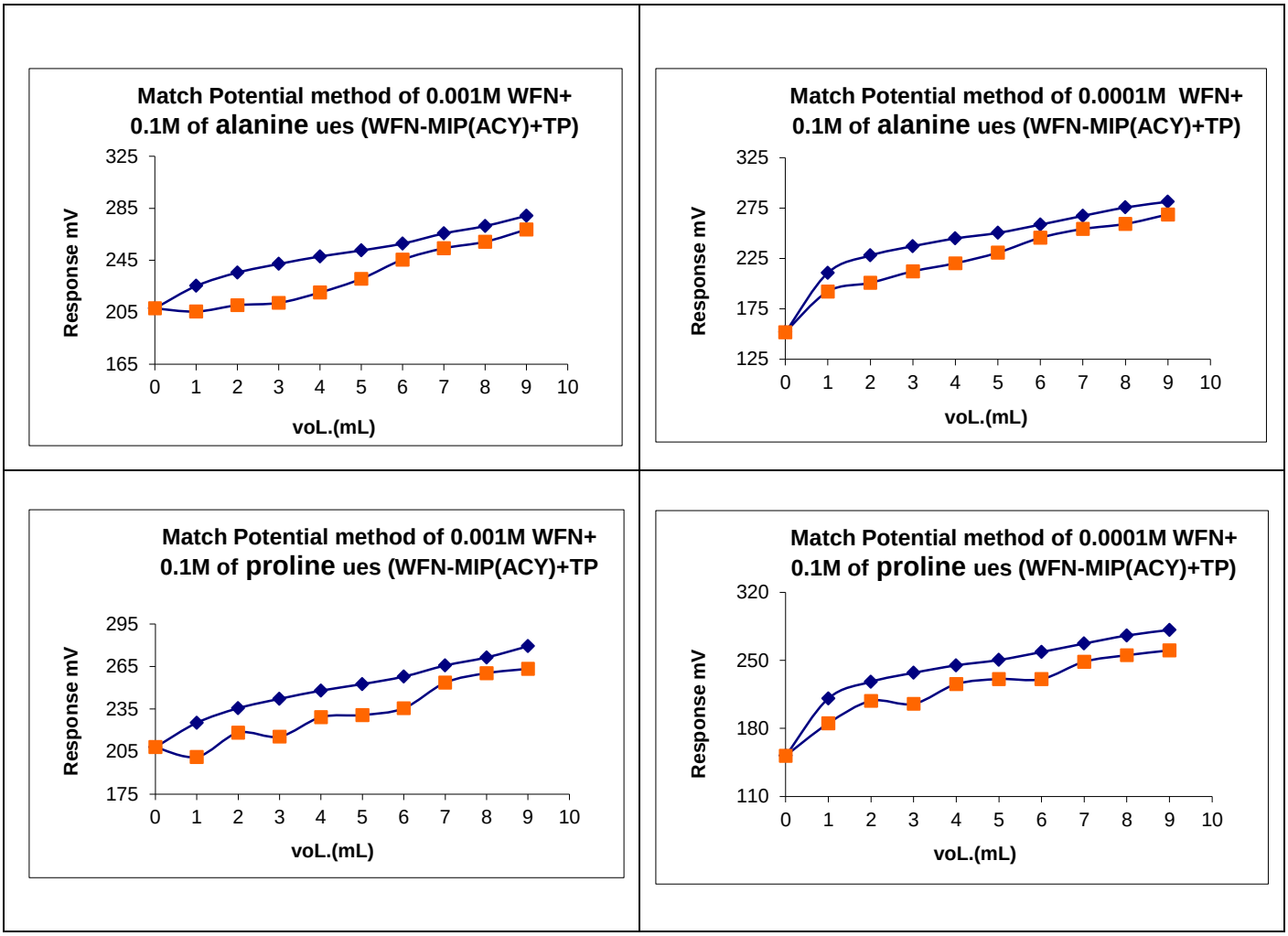


Figure (3.66) Selectivity of electrode for (10^{-3} and 10^{-4}) M based on TP, for cations interfering by match potential method, ■ Solutions of cations interfering ♦ WFN solutions.



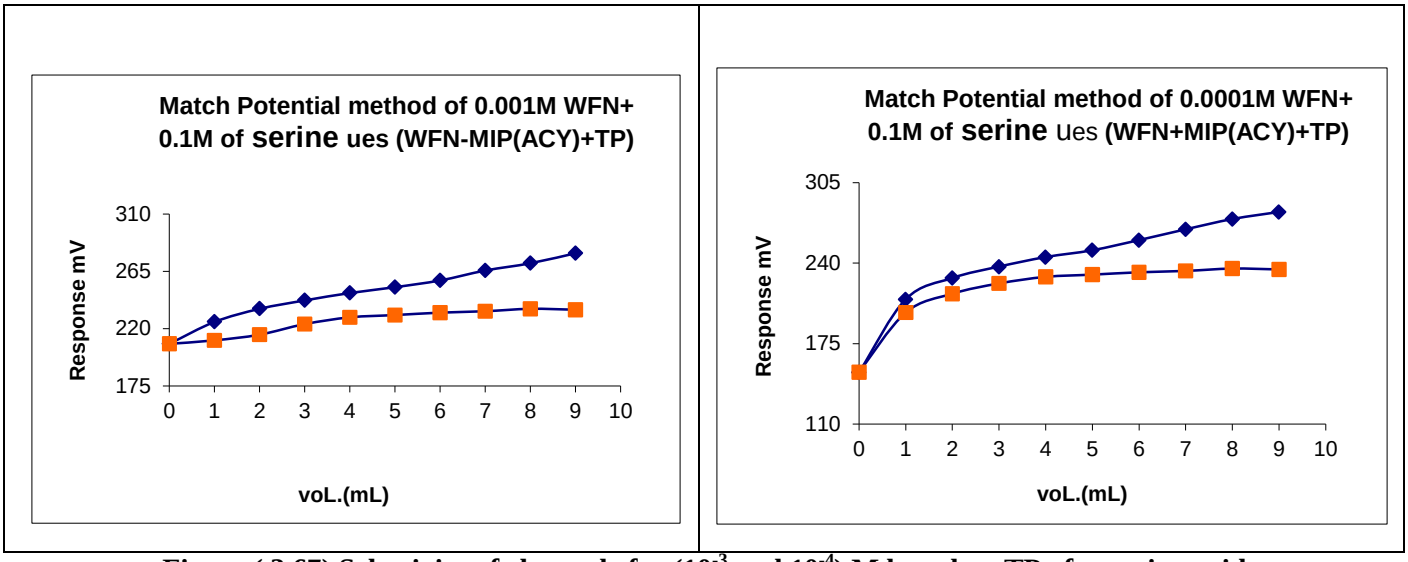
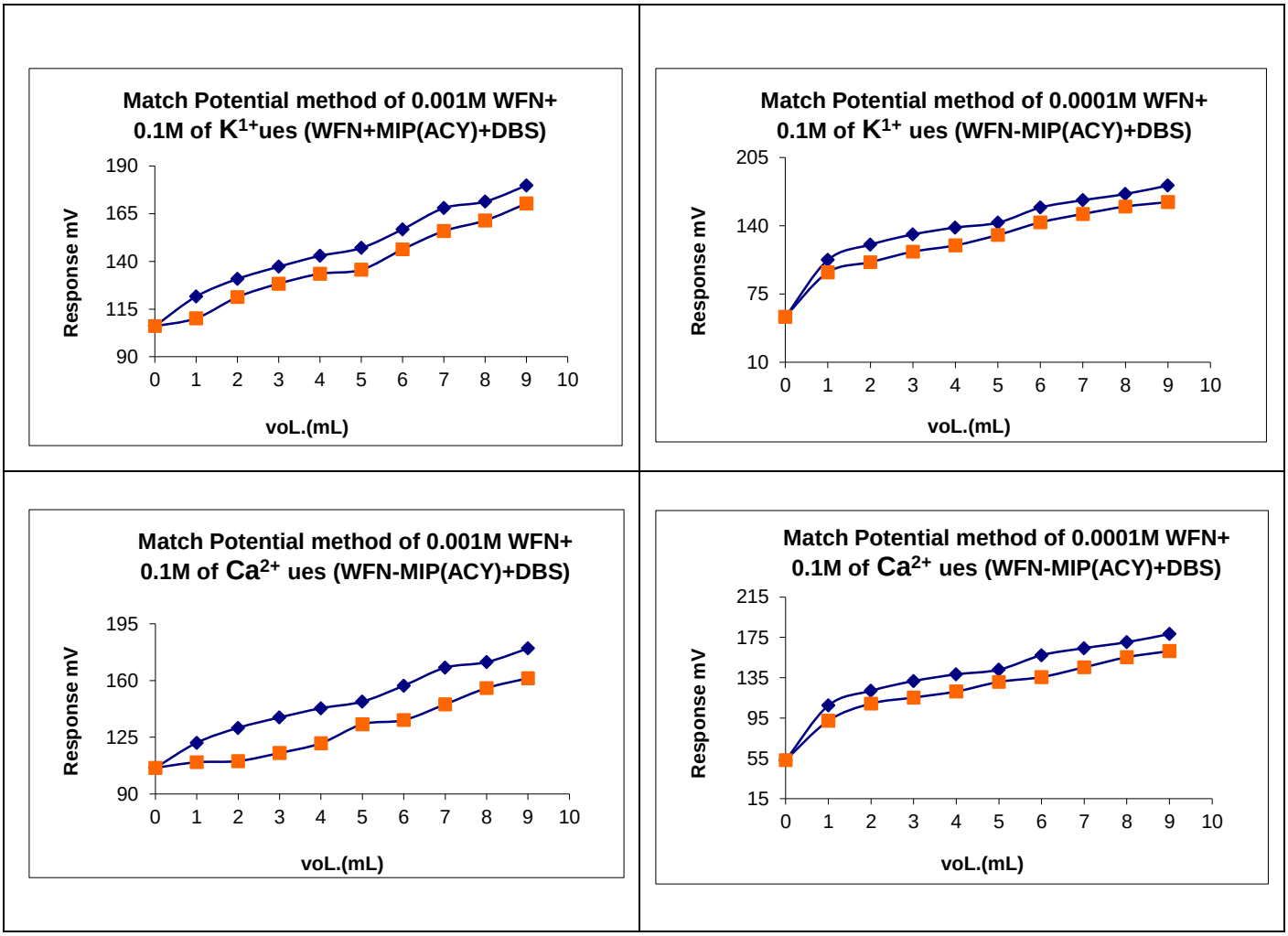


Figure (3.67) Selectivity of electrode for (10^{-3} and 10^{-4}) M based on TP, for amino acid interfering by match potential method, ■ Solutions of amino acid interfering ♦ WFN solutions.



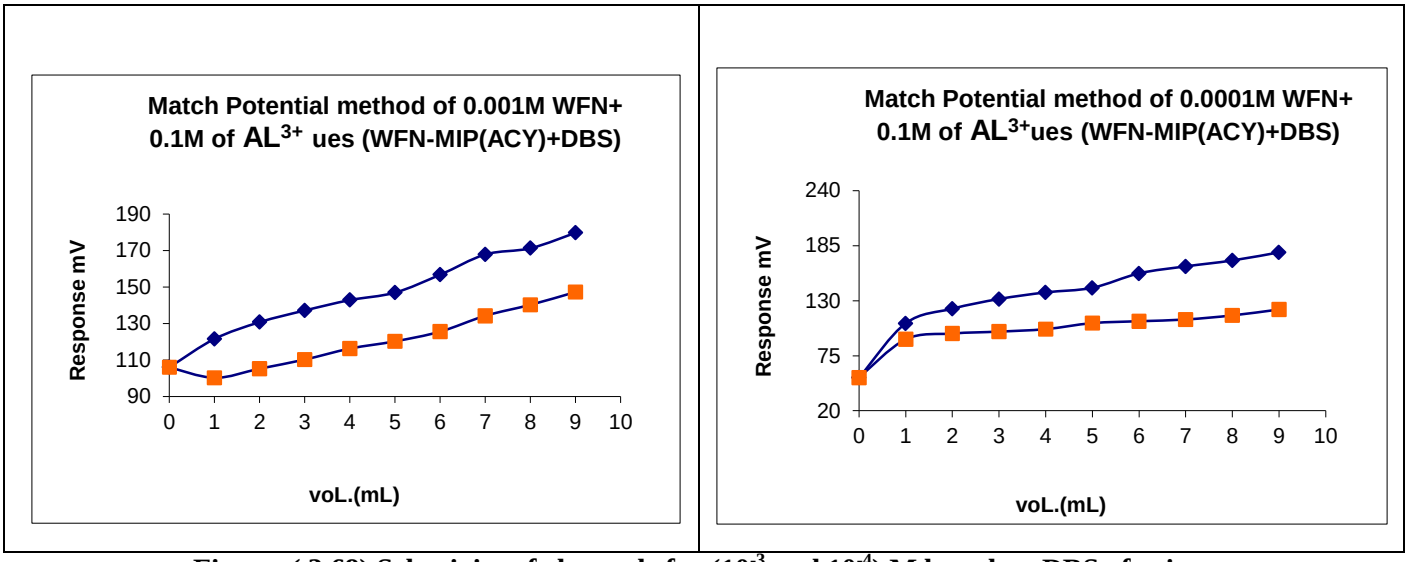
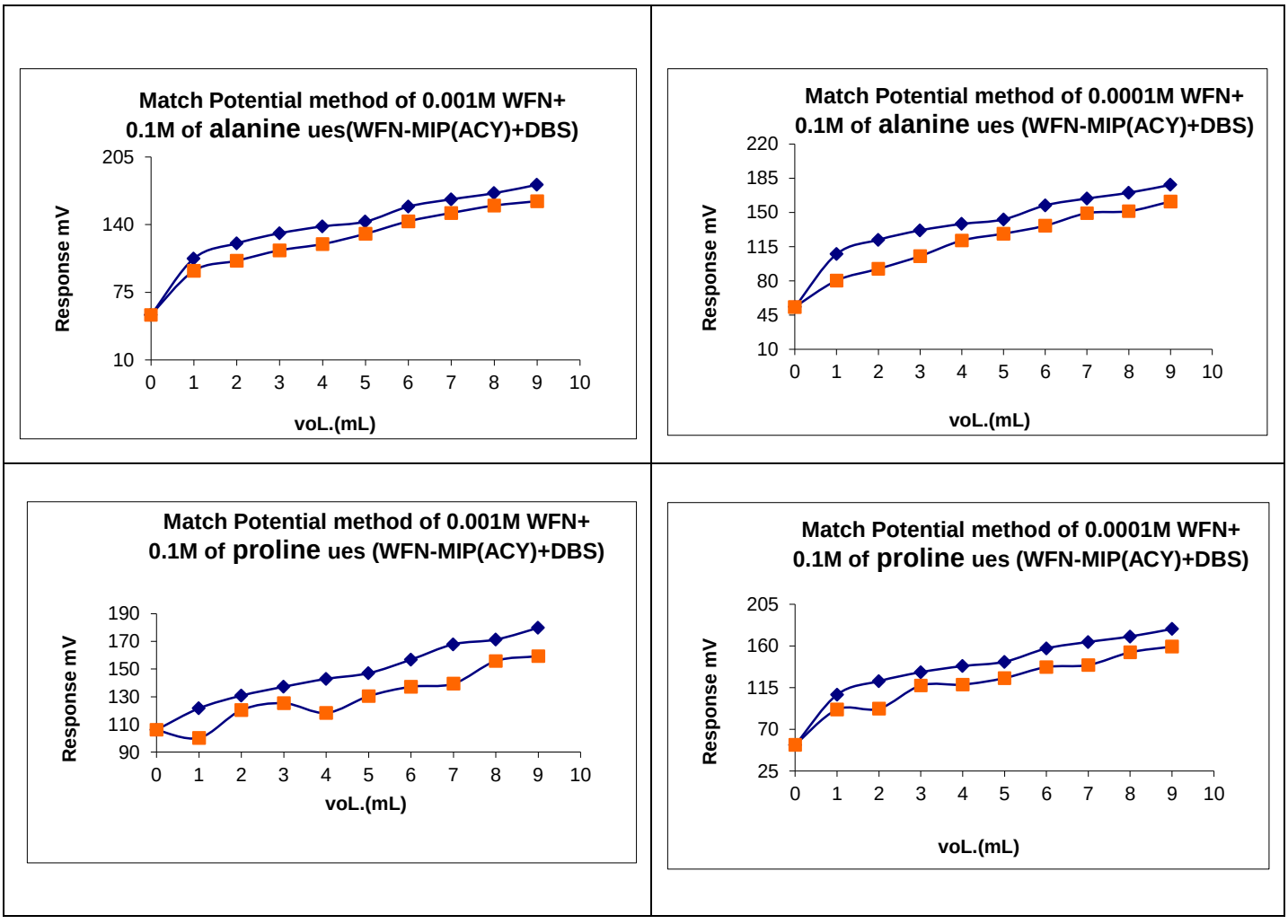
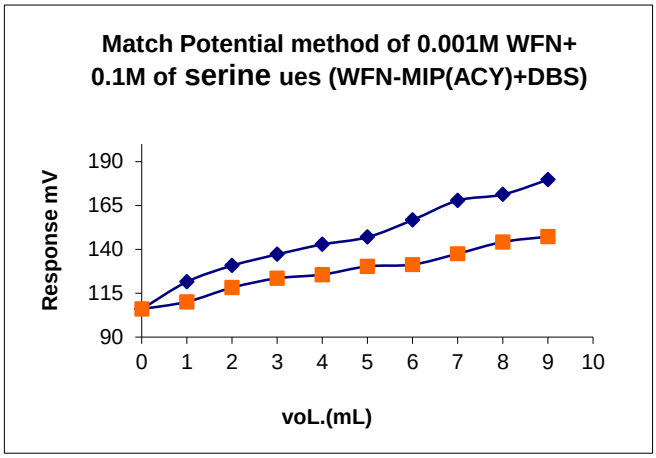


Figure (3.68) Selectivity of electrode for (10^{-3} and 10^{-4}) M based on DBS, for ions interfering by match potential method, ■ Solutions of cations interfering ♦ WFN solutions.





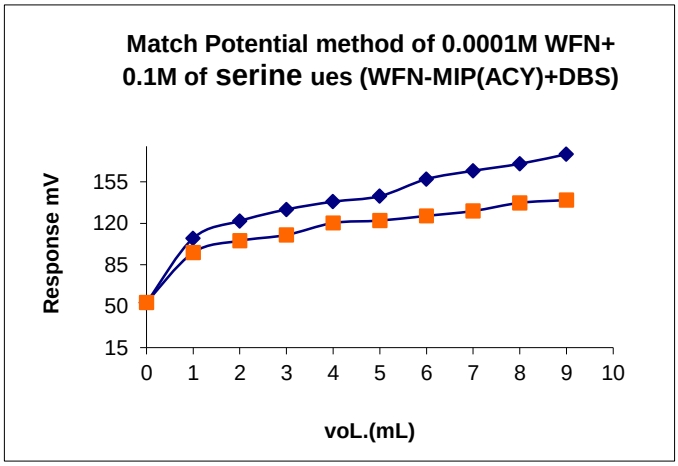
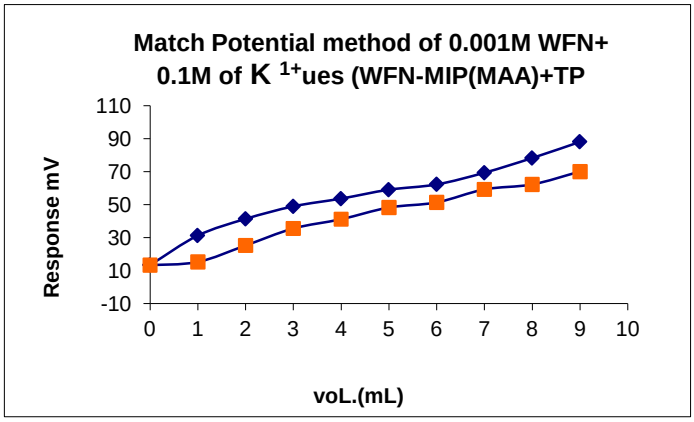
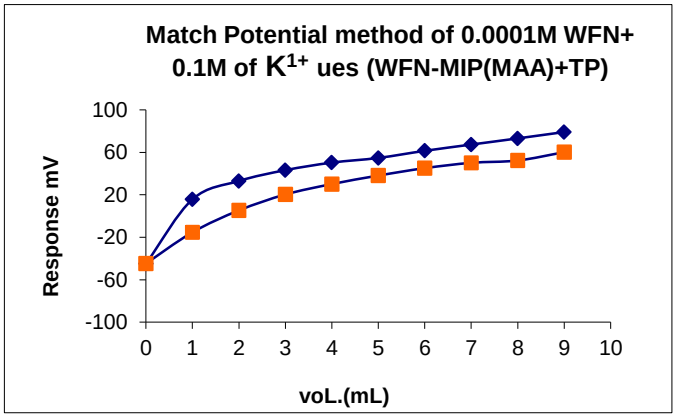
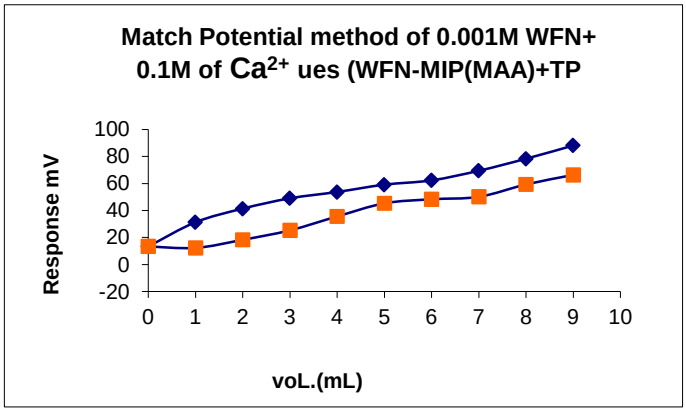
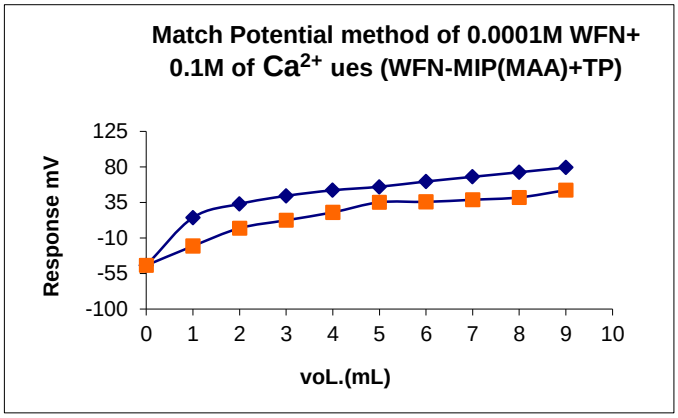


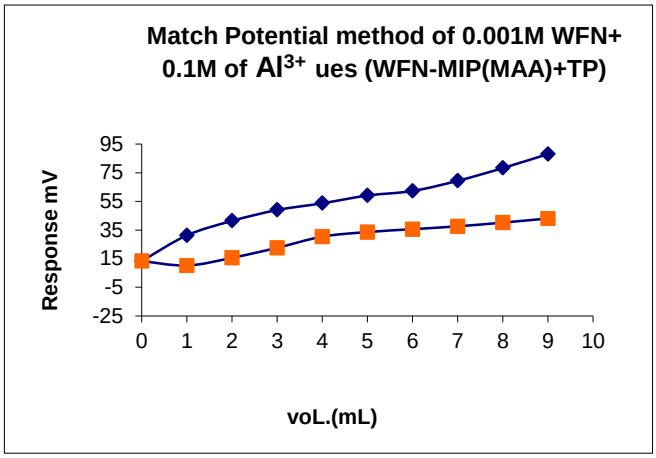
Figure (3.69) Selectivity of electrode for (10^{-3} and 10^{-4}) M based on DBS, for amino acid interfering by match potential method, ■ Solutions of amino acid interfering ♦ WFN solutions.











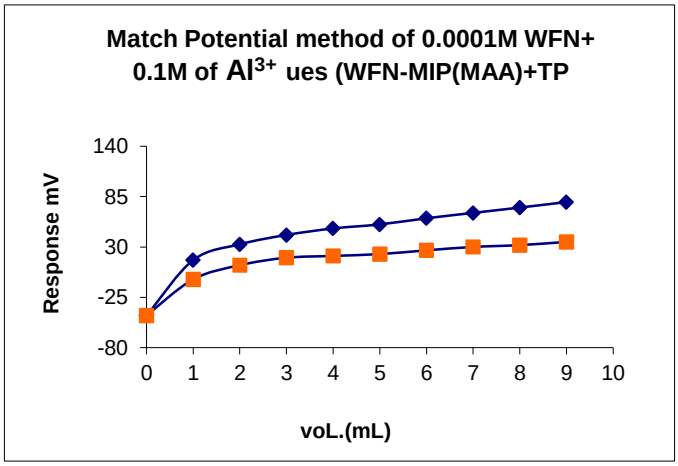
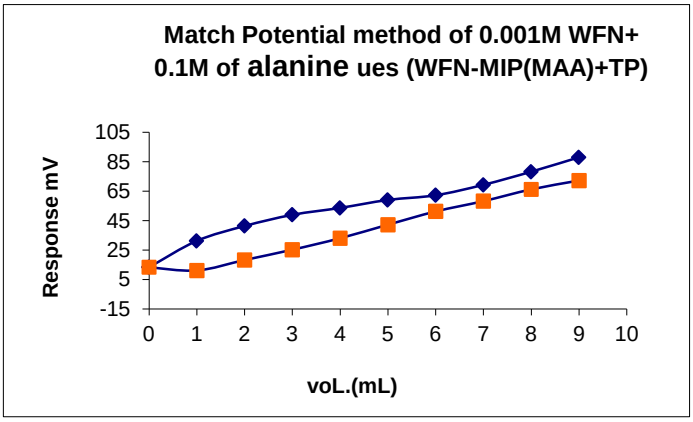
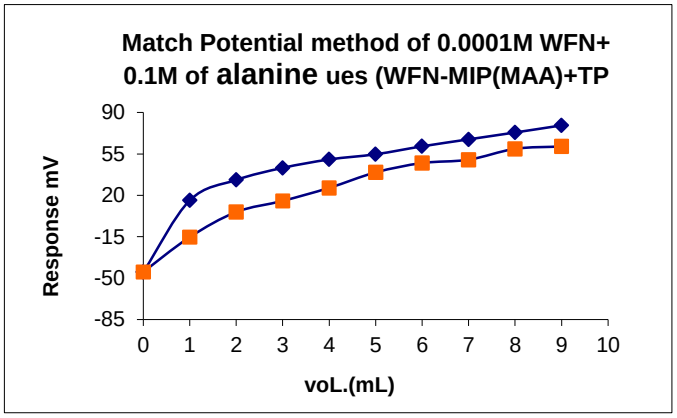
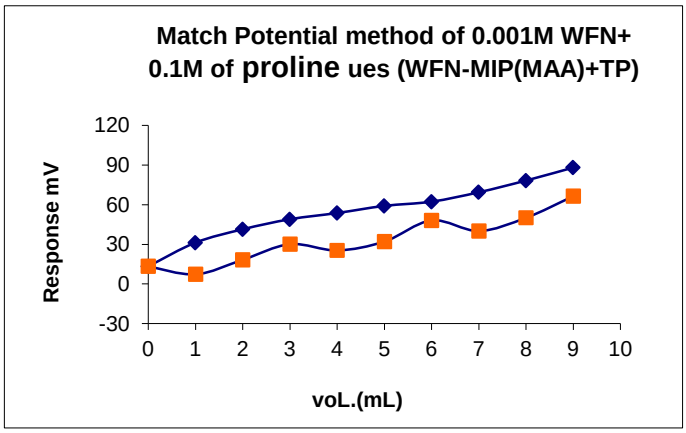
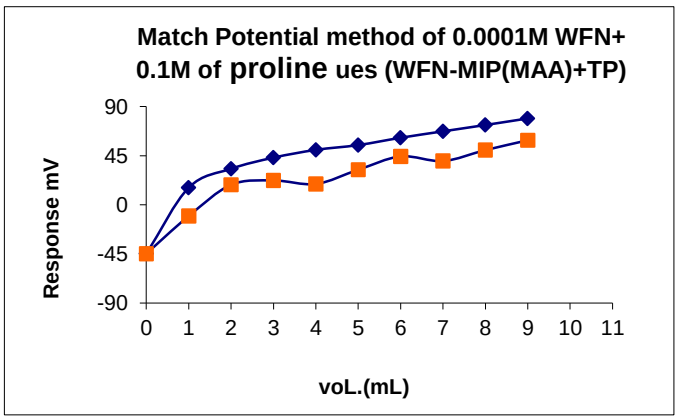


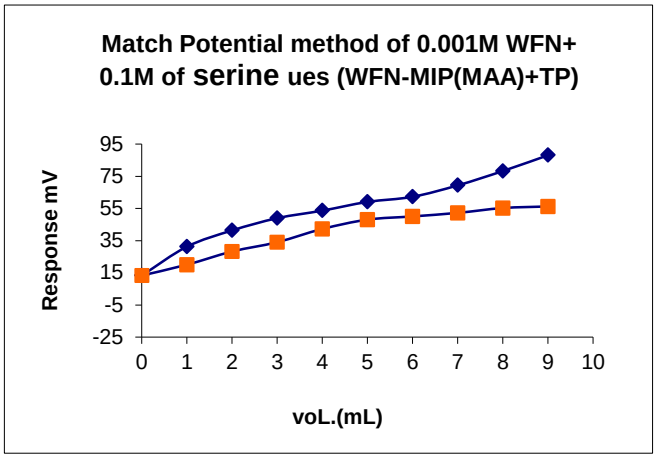
Figure (3.70) Selectivity of electrode for (10^{-3} and 10^{-4}) M based on TP, for ions interfering by match potential method, ■ Solutions of cations interfering ♦ WFN solutions.











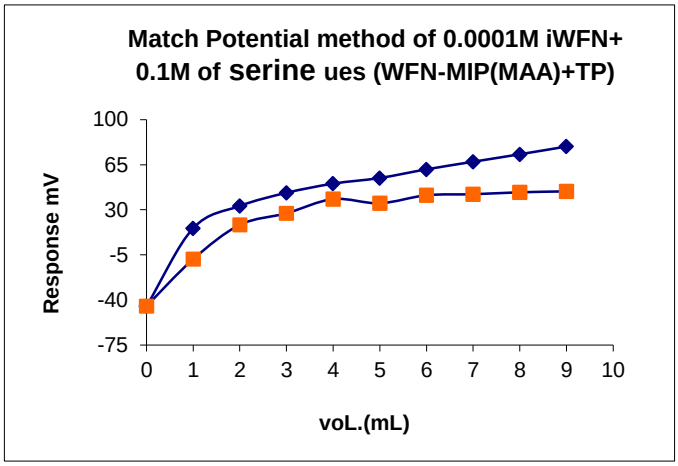
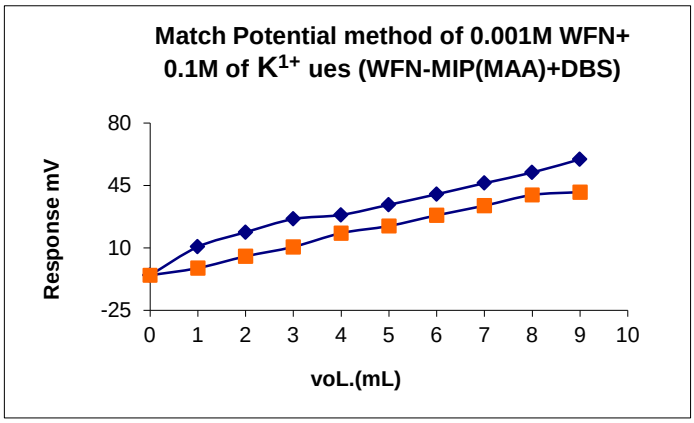
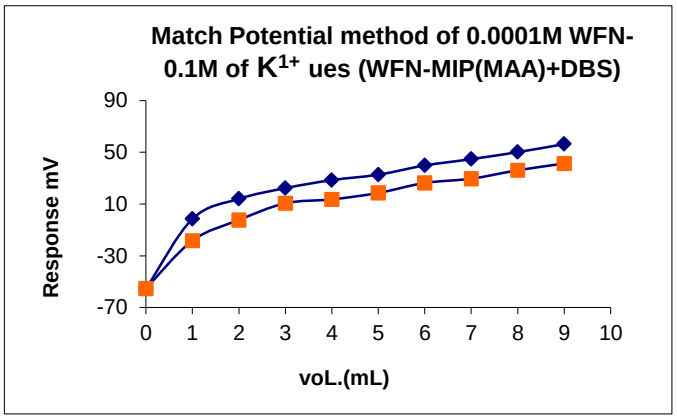
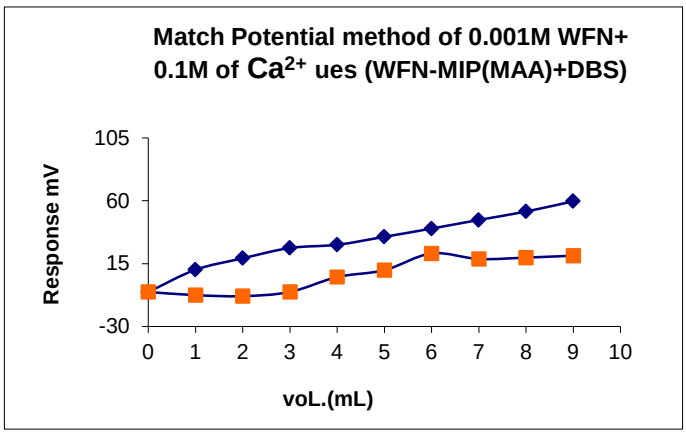
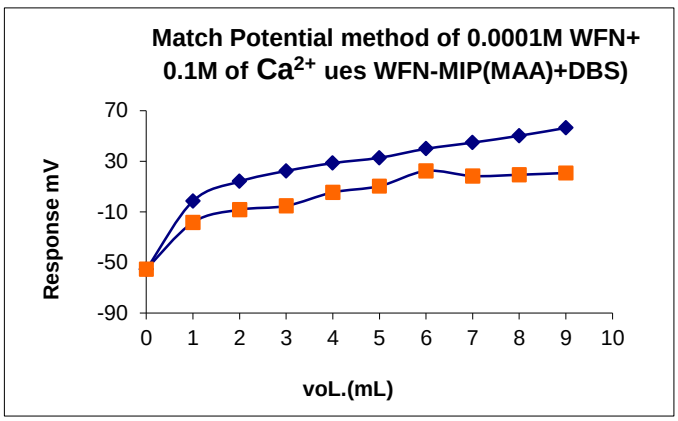


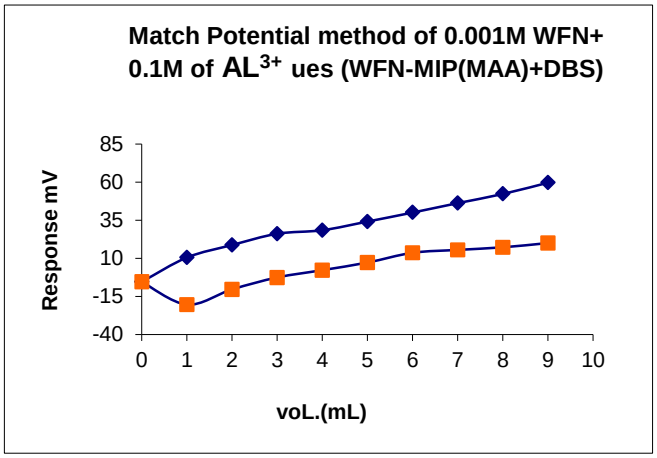
Figure (3.71) Selectivity of electrode for (10^{-3} and 10^{-4}) M based on TP, for amino acid interfering by match potential method, ■ Solutions of amino acid interfering ♦ WFN solutions.











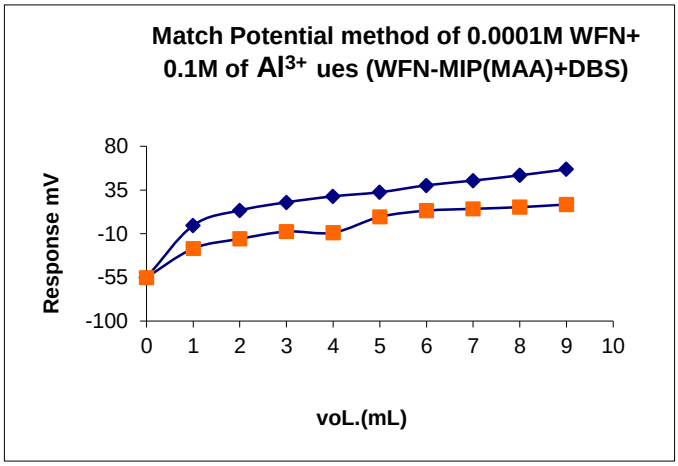
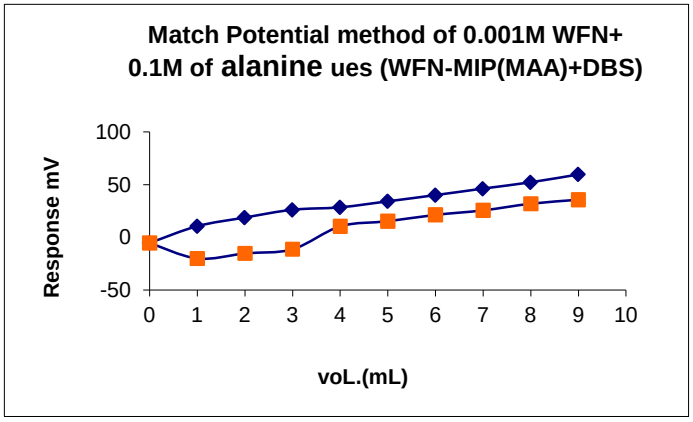
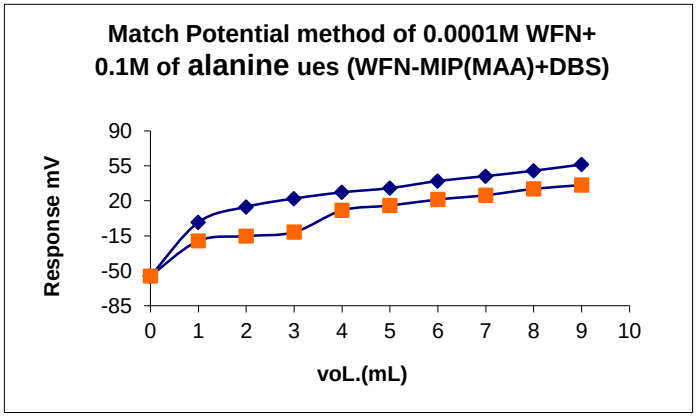
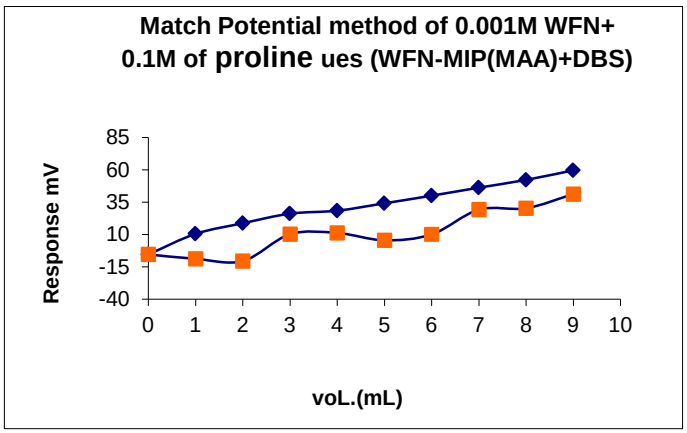
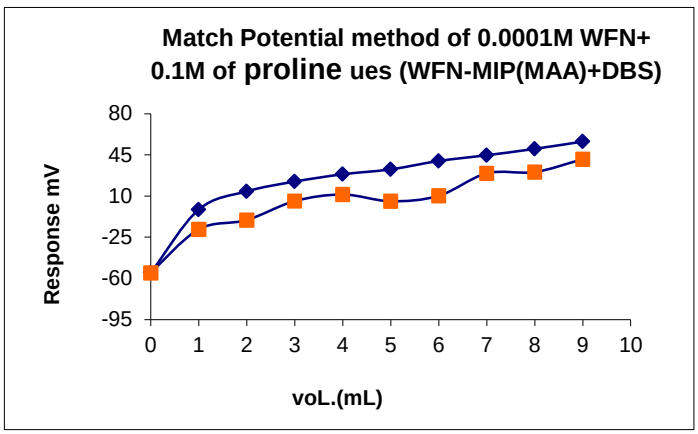


Figure (3.72) Selectivity of electrode for (10^{-3} and 10^{-4}) M based on DBS, for ions interfering by match potential method, ■Solutions of cation interfering ♦ WFN solutions.









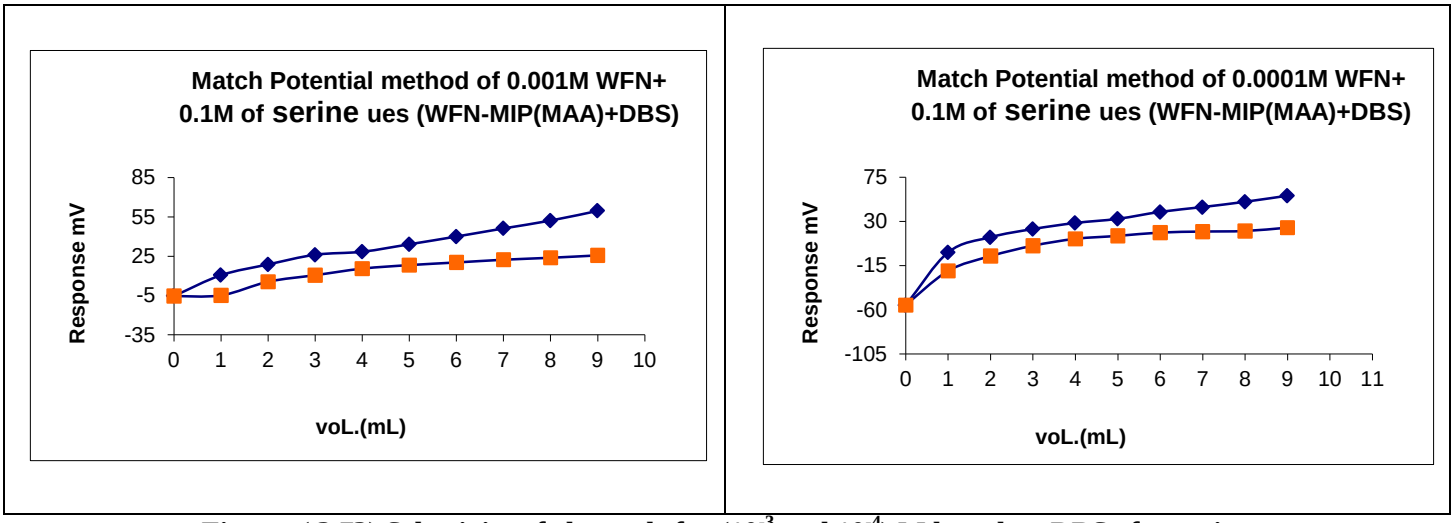


Figure (3.73) Selectivity of electrode for (10^{-3} and 10^{-4}) M based on DBS, for amino acid interfering by match potential method, ■ Solutions of amino acid interfering ♦ WFN solutions.

Table(3.72):selectivity cofficients for the WFN-MIP(ACY) electrodes and ($10^{-3,}$ 10^{-4}) M of interfering-ion determined by Match potential method (MPM).

Plasticizers	Interfering-Ion	K_{pot} at (10^{-3}) M	K_{pot} at (10^{-4}) M
WFN-MIP(ACY) +TP	K^+	3.661×10^{-1}	2.591×10^{-1}
	Ca^{2+}	2.112×10^{-1}	1.345×10^{-1}
	AL^{3+}	2.371×10^{-1}	1.241×10^{-1}
	Alanine	4.321×10^{-1}	1.253×10^{-1}
	Proline	4.289×10^{-1}	3.452×10^{-1}
	Serine	4.158×10^{-1}	3.122×10^{-1}
WFN-MIP(ACY) +DBS	K^+	2.333×10^{-1}	2.341×10^{-1}
	Ca^{2+}	2.151×10^{-1}	1.583×10^{-1}
	AL^{3+}	1.325×10^{-1}	1.427×10^{-1}
	Alanine	3.211×10^{-1}	6.352×10^{-1}
	Proline	4.267×10^{-1}	4.123×10^{-1}
	Serine	3.331×10^{-1}	3.243×10^{-1}

Table(3.73):selectivity cofficients for the WFN-MIP(MAA) electrodes and ($10^{-3,}$ 10^{-4}) M of interfering-ion determined by Match potential method (MPM).

Plasticizers	Interfering-Ion	K_{pot} at (10^{-3}) M	K_{pot} at (10^{-4}) M
WFN-MIP(MAA) +TP	K^+	1.283×10^{-1}	1.123×10^{-1}
	Ca^{2+}	1.235×10^{-1}	3.315×10^{-1}
	AL^{3+}	3.231×10^{-1}	3.328×10^{-1}
	Alanine	4.333×10^{-1}	2.213×10^{-1}
	Proline	5.281×10^{-1}	2.112×10^{-1}
	Serine	4.283×10^{-1}	4.333×10^{-1}
WFN-MIP(MAA) +DBS	K^+	3.825×10^{-1}	2.341×10^{-1}
	Ca^{2+}	2.311×10^{-1}	3.283×10^{-1}
	AL^{3+}	2.369×10^{-1}	1.125×10^{-1}
	Alanine	2.397×10^{-1}	5.235×10^{-1}
	Proline	3.147×10^{-1}	2.311×10^{-1}
	Serine	4.289×10^{-1}	3.233×10^{-1}

3.16. standard solution analysis:

The concentrations of solutions of warfarin sodium were determined using all the electrodes. Three potentiometric techniques were used for the determination of warfarin sodium namely direct, standard addition (SAM), and titration methods. The relative error RE% and relative standard deviation RSD% were calculate for each method.

3.16.1. Direct potentiometric method.

This is the simplest and most widely used method of obtaining quantitative result by using ion-selective electrode. The calibration curve was constructed and the concentration of the unknown was calculated by linear equation of the calibration curve the results are listed in table (3.82).

3.16.2.Calculation of Standard Addition Method SAM:

In this method concentrations of (10^{-3} and $10^{-4)}$ M for the four warfarin sodium electrodes using equation (1-10) are listed in Tables (3.74) to (3.81), The RSD% and RE % were calculate from the results obtained for each method are given in Table(3.82).

Table (3.74): Potential of 10^{-3}M WFN against the volume of standard warfarin sodium and the calculation of five additions using SAM. For WFN-ACY+ TP electrode.

V_S mL added	E/mV	*Antilog*E/S	Δ E	*Antilog*ΔE/S	(V_U/V_S)	C_U M
0	208.1	0.439×10^{4}	---	---	---	---
0.1	225.3	0.878×10^{4}	17.2	2.000	100	0.989×10^{-3}
0.2	235.6	1.330×10^{4}	27.5	3.029	50	0.976×10^{-3}
0.3	242.2	1.735×10^{4}	34.1	3.952	33.33	1.006×10^{-3}
0.4	248.0	2.192×10^{4}	39.9	4.993	25	0.991×10^{-3}
0.5	252.6	2.639×10^{4}	44.5	6.010	20	0.988×10^{-3}

Table (3.75): Potential of 10^{-4}M WFN against the volume of standard warfarin sodium and the calculation of five additions using SAM. For WFN-ACY+ TP electrode.

V_S mL added	E/mV	*Antilog*E/S	Δ E	*Antilog*ΔE/S	(V_U/V_S)	C_U M
0	151.9	0.455×10^{3}	---	---	---	---
0.1	210.8	4.895×10^{3}	58.9	10.739	100	1.025×10^{-4}
0.2	228.0	9.792×10^{3}	76.1	21.480	50	0.975×10^{-4}
0.3	237.2	14.188×10^{3}	85.3	31.123	33.33	0.995×10^{-4}
0.4	244.9	19.351×10^{3}	93.0	42.448	25	0.964×10^{-4}
0.5	250.4	24.153×10^{3}	98.5	52.983	20	0.960×10^{-4}

Table (3.76): Potential of 10^{-3}M WFN against the volume of standard warfarin sodium and the calculation of five additions using SAM. For WFN-ACY+ DBS electrode.

V_S mL added	E/mV	*Antilog*E/S	Δ E	*Antilog*ΔE/S	(V_U/V_S)	C_U M
0	106.1	1.064×10^{2}	---	---	---	---
0.1	121.6	2.105×10^{2}	15.5	1.977	100	1.013×10^{-3}
0.2	130.8	3.155×10^{2}	24.7	2.964	50	1.008×10^{-3}
0.3	137.2	4.181×10^{2}	31.1	3.928	33.33	1.014×10^{-3}
0.4	142.9	5.373×10^{2}	36.8	5.047	25	0.978×10^{-3}
0.5	147.0	6.435×10^{2}	40.9	6.045	20	0.981×10^{-3}

Table (3.77): Potential of 10^{-4}M WFN against the volume of standard warfarin sodium and the calculation of five additions using SAM. For WFN-ACY+ DBS electrode.

V_S mL added	E/mV	*Antilog*E/S	Δ E	*Antilog*ΔE/S	(V_U/V_S)	C_U M
0	53.2	0.103×10^{2}	---	---	---	---
0.1	107.4	1.127×10^{2}	54.2	10.852	100	1.013×10^{-4}
0.2	122.0	2.142×10^{2}	68.8	20.629	50	1.017×10^{-4}
0.3	131.7	3.282×10^{2}	78.5	31.608	33.33	0.979×10^{-4}
0.4	138.3	4.388×10^{2}	85.1	42.257	25	0.968×10^{-4}
0.5	142.9	5.373×10^{2}	89.7	51.736	20	0.984×10^{-4}

Table (3.78): Potential of 10^{-3}M WFN against the volume of standard warfarin sodium and the calculation of five additions using SAM. For WFN-MAA+ TP electrode.

V_S mL added	E/mV	*Antilog*E/S	Δ E	*Antilog*ΔE/S	(V_U/V_S)	C_U M
0	13.4	0.169×10^{1}	---	---	---	---
0.1	31.3	0.343×10^{1}	17.9	2.025	100	0.966×10^{-3}
0.2	41.4	0.511×10^{1}	28.0	3.027	50	0.977×10^{-3}
0.3	49.0	0.690×10^{1}	35.6	4.068	33.33	0.968×10^{-3}
0.4	53.7	0.830×10^{1}	40.3	4.897	25	1.016×10^{-3}
0.5	59.1	1.027×10^{1}	45.7	6.058	20	0.978×10^{-3}

Table (3.79): Potential of 10^{-4}M WFN against the volume of standard warfarin sodium and the calculation of five additions using SAM. For WFN-MAA+ TP electrode.

V_S mL added	E/mV	*Antilog*E/S	Δ E	*Antilog*ΔE/S	(V_U/V_S)	C_U M
0	-44.8	0.017×10^{1}	---	---	---	---
0.1	15.7	0.185×10^{1}	60.5	10.858	100	1.013×10^{-4}
0.2	33.0	0.367×10^{1}	77.8	21.476	50	0.975×10^{-4}
0.3	43.2	0.549×10^{1}	88.0	32.106	33.33	0.963×10^{-4}
0.4	50.3	0.726×10^{1}	95.1	42.476	25	0.963×10^{-4}
0.5	54.7	0.863×10^{1}	99.5	50.521	20	1.008×10^{-4}

Table (3.80): Potential of 10^{-3}M WFN against the volume of standard warfarin sodium and the calculation of five additions using SAM. For WFN-MAA+ DBS electrode.

V_S mL added	E/mV	*Antilog*E/S	Δ E	*Antilog*ΔE/S	(V_U/V_S)	C_U M
0	-5.3	0.079×10^{1}	---	---	---	---
0.1	10.6	0.160×10^{1}	15.9	2.027	100	0.964×10^{-3}
0.2	18.8	0.230×10^{1}	24.1	2.919	50	1.031×10^{-3}
0.3	26.2	0.320×10^{1}	31.5	4.056	33.33	0.972×10^{-3}
0.4	78.5	0.354×10^{1}	35.8	4.910	25	1.012×10^{-3}
0.5	34.2	0.457×10^{1}	39.5	5.788	20	1.033×10^{-3}

Table (3.81): Potential of 10^{-4}M WFN against the volume of standard warfarin sodium and the calculation of five additions using SAM. For WFN-MAA+DBS electrode.

V_S mL added	E/mV	*Antilog*E/S	Δ E	*Antilog*ΔE/S	(V_U/V_S)	C_U M
0	-55.3	0.008×10^{1}	---	---	---	---
0.1	-1.5	0.093×10^{1}	53.8	10.929	100	1.006×10^{-4}
0.2	14.0	0.186×10^{1}	69.3	21.768	50	0.962×10^{-4}
0.3	22.3	0.269×10^{1}	77.6	31.482	33.33	0.983×10^{-4}
0.4	28.5	0.354×10^{1}	83.8	41.472	25	0.987×10^{-4}
0.5	32.7	0.427×10^{1}	88.0	49.985	20	1.019×10^{-4}

3.16.3. Titration method:

The principle of Molecularly imprinted polymers electrodes titrations is based on the fact that in a stoichiometric reaction between two species in solution, the end point of the reaction is characterized by the total disappearance of one of the species or first appearance of a product of the reaction. Figure (3.74) and (3.75) shows the titration curves of 10^{-3} and10^{-4} M WFN sample with dodeca- molybdo phoshophoric Acid as a ligand solution. The RSD% , RC% and RE % were calculate and the results obtained for each method are given in Table(3.82).

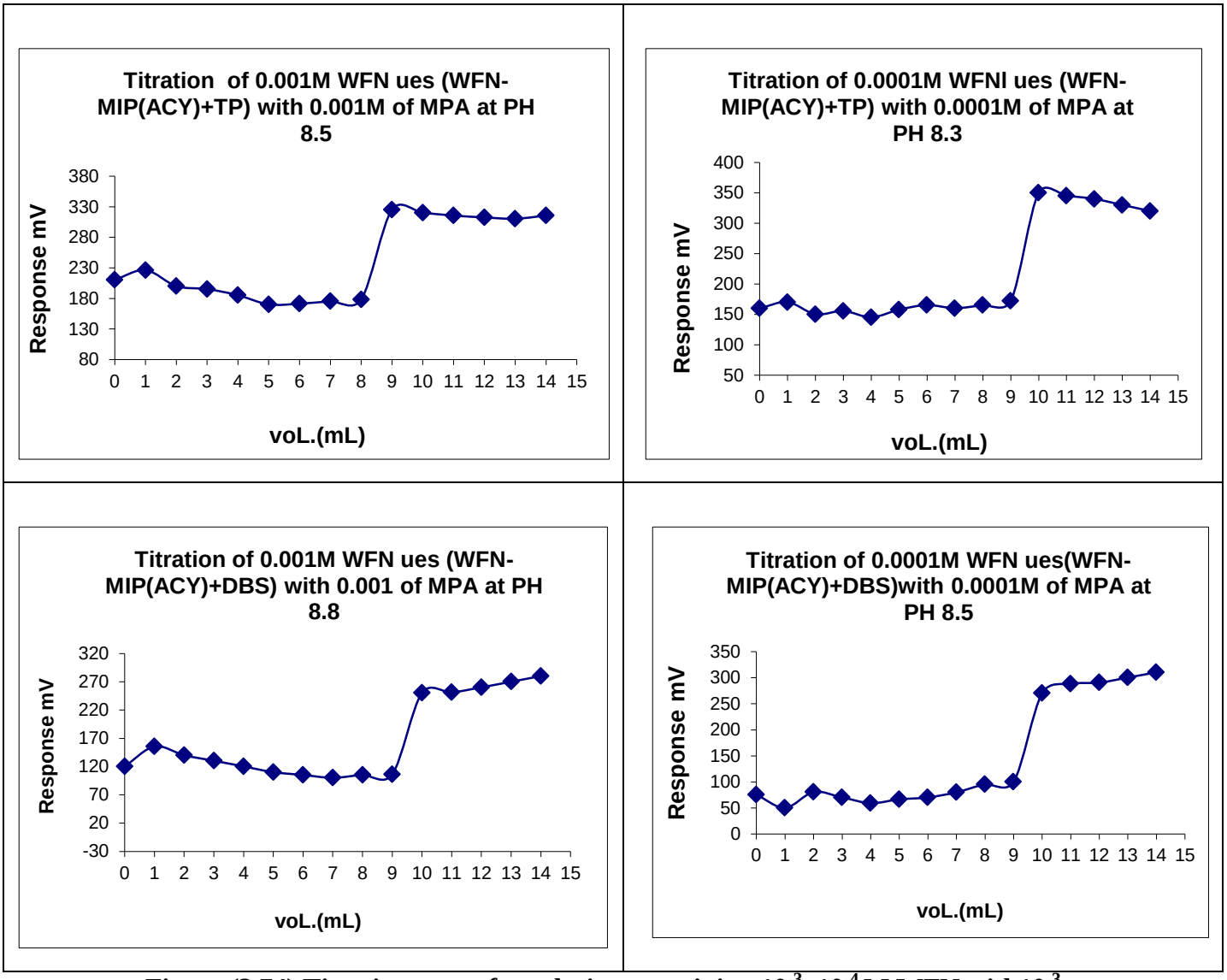


Figure (3.74) Titration curve for solution containing 10^{-3}, 10^{-4} M WFN with10^{-3}, 10^{-4} M PMA solution of electrode (WFN-MIP(ACY) by use TP,DBS as a plasticizer.

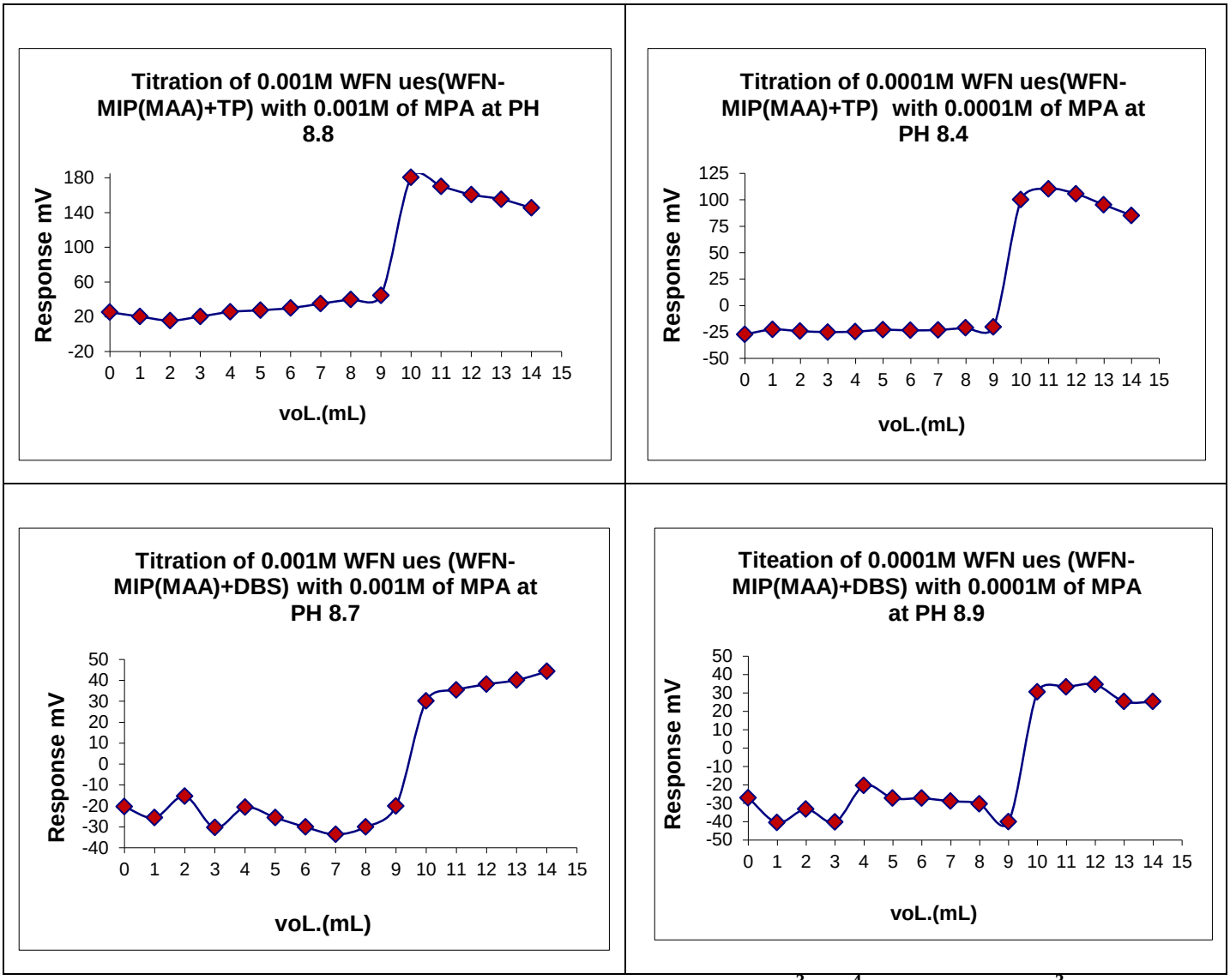


Figure (3.75) Titration curve for solution containing 10^{-3}, 10^{-4} M WFN with10^{-3}, 10^{-4} M PMA solution of electrode (WFN-MIP(MAA) by use TP,DBS as a plasticizer.

Table (3.82): Determination of warfarin sodium in the sample using WFN-MIPs electrodes.

Electrode No.	Concentrations (M)			
	Sample	Measurements using potentiometric methods		
		Direct	SAM	Titration
WFN-MIP(ACY)+TP (I)	1×10^{-3}	0.981×10^{-3}	0.990×10^{-3}	0.960×10^{-3}
	*RSD%	0.044	0.753	0.788
	RC%	98.1	99.0	96.0
	RE%	-1.9	-1.0	-4.0
	1×10^{-4}	1.018×10^{-4}	0.983×10^{-4}	0.975×10^{-4}
	*RSD%	0.057	0.987	1.231
	RC%	101.8	98.3	97.5
	RE%	1.8	-1.7	-2.5
WFN-MIP(ACY)+DBS (II)	1×10^{-3}	1.044×10^{-3}	0.998×10^{-3}	0.965×10^{-3}
	*RSD%	0.115	0.145	1.088
	RC%	104.4	99.8	96.5
	RE%	4.4	-0.2	-3.5
	1×10^{-4}	1.016×10^{-4}	0.992×10^{-4}	0.955×10^{-4}
	*RSD%	0.244	1.247	1.852
	RC%	101.6	99.2	95.5
	RE%	1.6	0.8	-4.5
WFN-MIP(MAA)+TP (III)	1×10^{-3}	0.967×10^{-3}	0.981×10^{-3}	0.977×10^{-3}
	*RSD%	0.744	0.619	1.551
	RC%	96.7	98.1	97.7
	RE%	-3.3	-1.9	-2.3
	1×10^{-4}	0.976×10^{-4}	0.984×10^{-4}	0.963×10^{-4}
	*RSD%	0.475	0.779	1.987
	RC%	97.6	98.4	96.3
	RE%	-2.4	-1.6	-3.7
WFN-MIP(MAA)+DBS (IV)	1×10^{-3}	0.967×10^{-3}	1.002×10^{-3}	0.955×10^{-3}
	*RSD%	1.025	1.093	1.507
	RC%	96.7	100.2	95.5
	RE%	-3.3	0.2	-4.5
	1×10^{-4}	1.050×10^{-4}	0.991×10^{-4}	0.970×10^{-4}
	*RSD%	0.299	1.078	1.211
	RC%	105.0	99.1	97
	RE%	5	-0.9	-3

***Each measurement repeated five times.**

3.17.MIPs Electrodes:

The electrodes (I,II,III and IV) show the potentiometric response When used to determination the warfarin sodium in pharmaceutical preparation by direct potentiometric method, standard addition method, and potentiometric titration method the result shown from Table (3.83) to (3.86).

Table (3.83): Sample analyses of pharmaceutical Orfarin (3 mg) using WFN-MIP(ACY)+TP electrode

Pharmaceutical	**Orfarin (3 mg)**		
	Direct	**SAM**	**Titration**
Concentration Prepared	**1×10^{-3}**	**1×10^{-3}**	**1×10^{-3}**
***Found**	0.977×10^{-3}	1.015×10^{-3}	0.955×10^{-3}
Recovery %	97.7	101.5	95.5
RE %	-2.3	1.5	-4.5
***RSD%**	0.141*	0.997*	0.911*
Fexperimental	11.5	9.8	13.2
F theoretical	19.2		
Pharmaceutical	**Orfarin (3 mg)**		
	Direct	**SAM**	**Titration**
Concentration Prepared	**1×10^{-4}**	**1×10^{-4}**	**1×10^{-4}**
***Found**	0.980×10^{-4}	1.022×10^{-4}	0.960×10^{-4}
Recovery %	98.0	102.2	96.0
RE %	-2.0	2.2	-4.0
***RSD%**	0.752*	1.022*	1.511*
Fexperimental	9.8	11.1	10.8
F theoretical	19.2		

Table (3.84): Sample analyses of pharmaceutical Orfarin (3 mg) using WFN-MIP(ACY)+DBS electrode

Pharmaceutical	**Orfarin (3 mg)**		
	Direct	**SAM**	**Titration**
Concentration Prepared	**1×10^{-3}**	**1×10^{-3}**	**1×10^{-3}**
***Found**	105.0×10^{-3}	1.009×10^{-3}	0.960×10^{-3}
Recovery %	105.0	100.9	96.0
RE %	5.0	0.9	-4.0
***RSD%**	0.366*	0.785*	1.121*
Fexperimental	8.7	13.2	14.3
F theoretical	19.2		
Pharmaceutical	**Orfarin (3 mg)**		
	Direct	**SAM**	**Titration**
Concentration Prepared	**1×10^{-4}**	**1×10^{-4}**	**1×10^{-4}**
***Found**	0.982×10^{-4}	1.010×10^{-4}	0.950×10^{-4}
Recovery %	98.2	101.0	95.0
RE %	-1.8	-1.0	-5.0
***RSD%**	0.544*	1.322*	1.991
Fexperimental	15.7	11.1	10.8
F theoretical	19.2		

Table (3.85): Sample analyses of pharmaceutical Orfarin (3 mg) using WFN-MIP(MAA)+TP electrode

Pharmaceutical	**Orfarin (3 mg)**		
	Direct	**SAM**	**Titration**
Concentration Prepared	**1×10^{-3}**	**1×10^{-3}**	**1×10^{-3}**
***Found**	0.960×10^{-3}	1.023×10^{-3}	0.970×10^{-3}
Recovery %	96.0	102.3	97.0
RE %	-4.0	2.3	-3.0
***RSD%**	1.112*	1.085*	1.855
Fexperimental	9.7	11.8	16.3
F theoretical	19.2		
Pharmaceutical	**Orfarin (3 mg)**		
	Direct	**SAM**	**Titration**
Concentration Prepared	**1×10^{-4}**	**1×10^{-4}**	**1×10^{-4}**
***Found**	1.030×10^{-4}	1.018×10^{-4}	0.960×10^{-4}
Recovery %	103.0	101.8	96.0
RE %	3.0	1.8	-4.0
***RSD%**	0.711*	1.088*	2.012
Fexperimental	13.3	11.1	17.9
F theoretical	19.2		

Table (3.86): Sample analyses of pharmaceutical Orfarin (3 mg) using WFN-MIP(MAA)+DBS electrode

Pharmaceutical	**Orfarin (3 mg)**		
	Direct	**SAM**	**Titration**
Concentration Prepared	**1×10^{-3}**	**1×10^{-3}**	**1×10^{-3}**
***Found**	1.037×10^{-3}	0.995×10^{-3}	0.950×10^{-3}
Recovery %	103.7	99.5	95.0
RE %	3.7	-0.5	-5.0
***RSD%**	1.215*	1.222*	1.711
Fexperimental	12.3	9.7	14.9
F theoretical	19.2		
Pharmaceutical	**Orfarin (3 mg)**		
	Direct	**SAM**	**Titration**
Concentration Prepared	**1×10^{-4}**	**1×10^{-4}**	**1×10^{-4}**
***Found**	0.950×10^{-4}	1.011×10^{-4}	0.966×10^{-4}
Recovery %	95.0	101.1	96.6
RE %	5.0	1.1	-3.4
***RSD%**	0.311*	1.155*	1.279
Fexperimental	11.3	15.6	10.9
F theoretical	19.2		

*Each measurement repeated three times.

3.18.Conclusion:

Warfarin sodium which know as an anticoagulant drug determined in this work by used ISEs method and MIPs method.These methods are rapid, simple and accurate, the resulting F test obtained by ISEs and MIPs were quite comparable with HPLC as standard method in British pharmacopeia. The work included two part, the first part include ISEs method included fabrication of membranes for warfarin sodium were constructed by Dodeca-molybdo Phosphoric acid (MPA) and Dodeca–Phosphotungstic acid (PTA) with drug as ion-exchanger and many plasticizers : oleic acid (OA), tri-n-butylphosphate(TBP), Nitrobenzen (NB), Acetophenone (AP) and di-octyl phthalate (DOPH) in PVC matrix membranes.The best electrode for warfarin sodium by used oleic acid (OA) for each ion-exchanger . The second part included MIPs which used fabrication of membranes for warfarin sodium were constructed by Acrylamide (ACY)and Meth acrylic acid (MAA) as monomers and Ethylene glycol dimethacrylate(EGDMA) as cross-linker with drug as ion-exchanger and two plasticizer : Tritolyl phosphate (TP), Di butyl sebacate (DBS) in PVC matrix membranes the best electrode for warfarin sodium was (WFN-MIP(ACY),WFN-MIP(MAA)) by use TP as a plastisizer.

Future work

1. Prepared MIPs can be used as columm packing material for HPLC method.
2. Different plasticizers could be examined to get better idea on their influence on the electrode performance.
3. Other amount and percent of components proportions in membrane, through fixing one of the components and changing the other.
4. Study the selectivity behavior using other methods and also by using more interfering ions.
5. Other matrix used such as (Polyurethane and Silicone rubber) instead PVC in order to compare with PVC matrix.
6. Application of these membranes in analyses of other drug samples with similar active groups.
7. Use the Molecularly Imprinted polymers (MIPs) for determination of other drugs used different cross linker.

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الخلاصة

الرسالة تشمل ثلاث فصول رئيسية:

الفصل الاول: ويتضمن مقدمة عن تقنية الاقطاب الانتقائية ،كيفية عملها ،خصائصها، تصنيفها ،تصميم الاقطاب الانتقائية ومميزاتها مثل الانتقائية ومعامل الانتقائية وقياسها باستخدام طرق مختلفة منها (طريقة المحاليل المنفصلة) و (طريقة التطابق الجهدي) وكذلك معرفة مدى الخطية ،حد التحسس وزمن الاستجابة.

وكذلك تم الشرح عن موضوع الطبعة الجزيئية البوليمرية (الطريقة التساهمية والطريقة الغير التساهمية)، مكوناتها والعوامل المؤثرة على البلمرة (جزيئة البلمرة ،المجموعة الفعالة للمونمر، مواد التشابك ، البادئ و المذيب).العوامل التي تساعد على السيطرة على عملية البلمرة باستخدام طريقتين (البلمرة الثقيلة والبلمرة الترسيبية) ،والطرق المستخدمة في تقدير الدواء بطريقة الاقطاب الانتقائية وطريقة الطبعة الجزيئية هي الطريقة المباشرة ،طريقة الاضافات القياسية ،طريقة الاضافات القياسية المتعددة والطريقة التسحيحية .ويشمل هذا الفصل مسح شامل للبحوث التي لها علاقة بهذا الموضوع .

الوارفرين صوديوم هو دواء مضاد للتخثرونظرا لقدرته البايولوجية وتكوين المعقدات فهو يقلل من عملية التخثر.

الفصل الثاني : يعطي هذا الفصل وصف كامل للمواد الكيميائية المستخدمة ،كيفية تحضيرهم ،بالاضافة الى الاجهزة والمعدات ،تصميم الخلية ، تحضيربوليمرات الطبعة الجزيئية وصب الغشاء.

الخلاصة

الفصل الثالث :ويتألف من طريقتين :

1-الاقطاب الانتقائية الايونية .

تم تحضير الاقطاب النتقائية الايونية لدواء الوارفرين صوديوم بالاعتماد على

Dodeca-molybdo Phosphoric acid (MPA) , Dodeca–Phosphotungstic acid (PTA) وباستخدام عدة ملدنات منها :

oleic acid (OA), tri-n-butylphosphate(TBP), Nitrobenzen (NB), Acetophenone (AP) and di-octyl phthalate (DOPH) باستخدام قالب PVC.

تم بناء الغشاء عن طريق خلط كميات مناسبة من الملدن مع معقد الدواء باستخدام PVC .

الاقطاب المحضرة تضمنت دراسة كلا من مدى التراكيز ،الميل ،حد التحسس ، عمر القطب ، معامل الارتباط والدالة الحامضية ، وكذلك التداخلات تم دراستها مع الايونات الاحادية والثنائية والثلاثية مثل (K^+, Na^+,Ca^{2+} ,Mg^{2+},Al^{3+},Fe^{3+}) وكذلك استخدمت الاحماض الامينية مثل (Alanine, Proline , Serin) والدراسة تمت باستخدام طريقة المحاليل المنفصلة وطريقة التطابق الجهدي لايجاد معامل التداخل .الاقطاب المحضرة من (WFN-MPA+OA WFN-MPA+TBP, WFN-MPA+NB ,WFN-MPA+AP,WFN-MPA+DOPH) اعطت مدى خطية بين (1×10^{-5} -1×10^{-1}) مولاري مع ميل نرنيستي (21.28–31.57) ملي فولت /حقبة وحد تحسس (7×10^{-6} - 2×10^{-5}) مولاري وكان عمر الاقطاب بين (7-35) يوم ومعامل الارتباط (0.9998 - 0.9969) على التوالي .الدالة الحامضية كانت محصورة بين (2.5 – 10.0) .

اما الاقطاب المحضرة من , WFN-PTA+OA, WFN-PTA+TBP, WFN-PTA+NB WFN-PTA+AP , WFN-PTA+DOPH اعطت مدى خطية بين (1×10^{-5} –1×10^{-1}) مولاري وميل نرنستيني (29.62_ 20.04) ملي فولت/حقبة وحد تحسس (6×10^{-6} _ 4×10^{-5}) مولاري وعمرالاقطاب كان بين (40 - 10) يوم ومعامل الفعالية بين (0.99949- 0.9984) على التوالي .وكانت الدالة الحامضية بين (3.5 – 10.0).

وقد استخدمت الاقطاب المذكورة اعلاه في تعيين دواء الوارفرين صوديوم في المستحظرات الصيدلانية.

2-الطبعة الجزيئية البوليمرية : في هذه الطريقة تم تحضير طبعة جزيئية لدواء الوارفرين صوديوم باستخدام اكريلا امايد و حامض اكريلك كمونيمرات واثلين كلايكول داي مثيل اكريليت كمادة تشابك و بنزويل بيروكسيايد كمادة بادئ .وتم استخدام نوعين من الملدنات هي

(Tritolyl phosphate (TP), Di butyl sebacate (DBS) وPVC كقالب للغشاء .

حضرت الاقطاب من خلط كميات من الملدنات مع المادة البوليمرية باستخدام PVC كقالب للغشاء. وتضمنت الدراسة مدى التركيز ،الميل ، حد التحسس ،عمر القطب ،معامل الارتباط ومدى الدالة الحامضية ،كذلك تم دراسة التداخلات مع الايونات الاحادية والثنائية والثلاثية مثل (K^+ ,Ca^{2+} , Al^{3+}) بالاضافة الى الاحماض الامينية مثل (Alanine,Proline,Serine) باستخدام طريقتي المحاليل المنفصلة وطريقة التطابق الجهدي لايجاد معامل التداخل .القطاب المحضرة من WFN-MIP(ACY)+TP، WFN-MIP(ACY)+DBS ،

WFN-MIP(MAA)+TP،WFN-MIP(MAA)+DBS اظهرت مدى استجابة بين

(1×10^{-1} -1×10^{-5})مولاري مع ميل (51.80-58.41) ملي فولت/حقبة وحد التحسس كان

(4×10^{-6} - 3×10^{-5})مولاري وعمر الاقطاب كان بين (30-45) يوم ومعامل الارتباط بين

(0.9996 - 0.9987) بالتوالي وكانت الدالة الحامضية محصورة بين (9.5 – 3.5) .

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

بناء اقطاب انتقائية جديدة -الطبعة الجزيئية البوليمرية لدواء ورفارين صوديوم

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

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