A Sensitive Electrochemical Sensor for Rapid Determination of Mebeverine Hydrochloride and Metronidazole Benzoate Selective Molecular Imprinted Polymer in the PVC Membrane

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Abstract

By using precipitation polymerization, liquid electrodes of polymers imprinted with Mebeverine hydrochloride and metronidazole benzoate were created whereas the imprinted polymer (MIP) and non-imprinted (NIP) polymers were prepared by using Mebeverine hydrochloride and Metronidazole benzoate qua a template. In the polymerization process, 2-Acrylamido-2-methyl-1-propane Sulphonic acid (AMPS) or 1-Vinylimidazole (VIZ) was used qua monomer, pentaerythritol triacrylate (PETRA) or Divinylbanzene (DVB) was used qua a cross-linker while benzoyl peroxide (BPO) was used as an initiator. The MIP membranes and the membranes of NIP were created by using Dibutyl Sebacate (DBS) and Tris(2-ethylhexyl) phosphate(TEHP) qua plasticizers in PVC matrix. The response time of the liquid electrodes was 1min. whereas their slopes and detection limits reached to 19.62 – 57.36 mV per decade and 1.2 x 10^{-6} – 2.0 x 10^{-5} M, respectively. Filling with standard solution of drug (0.1M), the liquid electrodes response -with suitable No. (selectivity for numerous of species - was suitable No. (since pH reached to 1.5 – 12. The developed electrodes were successfully applied for the analyte determination in preparation pharmaceutical sample without any time consuming pretreatment steps.

Keywords: molecularly imprinted electrodes, Mebeverine hydrochloride, Metronidazole benzoate, 2-Acrylamido-2-methyl-1-propane sulphonic acid monomer.

Introduction

As one of the nitroimidazole derivative, Metronidazole benzoate(MNZB), figure (1)1-(2-benzyloxy ethyl)-5-nitro methylimidazole is recognized for its antimicrobial features as this compound is effective before trichomonas, anaerobic bacteria and Vincent's organisms. MNZB is used by Veterinarians to medicate infected dogs and cats with giardia and other bacterial infections [1]. Numerous analytical procedures have been stated for identifying MNZB figure (1) presents its chemical structure), including spectrophotometry [2], gas chromatography [3], and high performance liquid chromatography [4]. Nevertheless, the cited methods have un-sufficient selectivity for MNZB identification. Therefore, developing an alternative procedure to determine MNZB with a high sensitivity and selectivity become essential goal.

Mebeverine hydrochloride (MBV)[3,4-Dimethoxybenzoic acid 4-[ethyl[2-(4-methoxyphenyl)-1-methylethyl]amino]-butylester] figure (2) is an active antispasmodic drug. it effects at most smooth gastrointestinal muscles as well as it in particular treats the colonic spasm [5]. This drug is presystemic hydrolysis in the gut and/or the liver rapidly and extensively [5]. British Pharmacopoeia explains the properties of a non-aqueous titrimetric procedure for identifying the MBV in synthesis form [6]. Various spectrophotometric [7–13], electrochemical [14–16] and chromatographic procedures [17–25] were stated since they are adopted for identifying the MBV in pharmaceutical production and biological fluids.

Imprinted polymer is a controversial procedure used widely to create synthetic molecular receptors which is much efficient.

Recently, this technique has been developed to be very advantageous complementary concept in the analytical chemistry regarding the biological identification with increased applicability, providing an inexpensive and versatile platform for producing a polymer matrix with molecule-specific identification features with wide range applications including but not limited to purificating the racemic mixtures, chemical sensing and catalytic control of complex chemical reactions [21]. Many researches available on the subject much emphasize the 'biomimetic' features manifested by MIP with the substrate-selective mechanisms being equivalent to that of natural entities like antibodies and enzymes.

The lock-and-key mechanism which was supposed by Emil Fischer, noble laureate, was demonstrating enzyme–substrate interaction; in fact, the concepts of MIP theory are the best equivalent example of this mechanism in biochemistry [22]. MIP theory offered that enzymes have more flexible substructure than that specified by the lock-and-key theory. Nevertheless, the concept of a matrix that is originated to identify a particular substrate still the strong basic part of MIP theory figure (3). This idea has been the main objective of research in the field of chemistry since the key reappearance of interest in MIP in the 1970.

Recently, the MIP technology has got much attention that has documented in numerous comprehensive publications discussed deeply the relative advantages and disadvantages of this technology [23-25] [21 and 26]. Some of these publications present quantitative analytical methods using MIPs in detail, but selective analyze retention for qualitative purposes already finds more extensive application. However, to understand the dominant mechanisms of producing selectivity in molecular imprinted polymers at a molecular level, more studies and researches shall be conducted on the development of improved MIP technology with enhanced identification features.

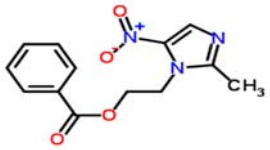


Figure (1): Metronidazole Benzoate

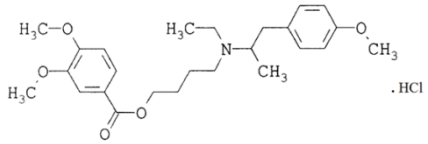


Figure (2): Structural formula of Mebeverine

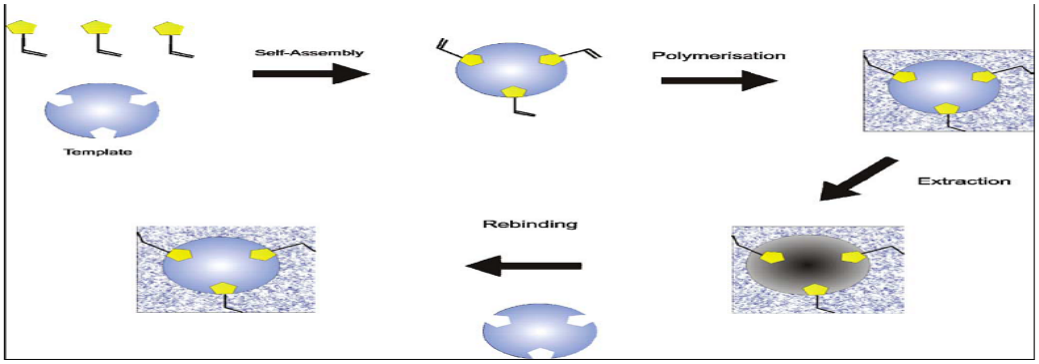


Figure (3): Schematic representation of non-covalent imprinting.

Experimental

material and reagent

Mebeverine hydrochloride and Metronidazole benzoate were obtained from the SDI Company located at Iraq, Samarra. Tris (2-ethylhexyl) phosphate(TEPH) and Di-Butylsebacate (DBS) and metal salts were bought from Sigma-Aldrich. Pentaerythritoltriacrylate(PETRA) (99%), 2-Acrylamido2-methyl-1-propane sulphonic acid(AMPS)(99%),(2-Acrylamido-2-methyl-1-propane Sulphonic acid (AMPS) (99%), (or (1-Vinylimidazole) (99%), (pentaerythritol triacrylate (PETRA) or Divinylbanzene) and benzoyl peroxide (BPO) (78%) were purchased from Sigma-Aldrich. The highest purity chemicals were reagent value.

Apparatus

Potentiometric measurements were carried out with a digital voltmeter (HANA pH 211 instrument Microprocessor pH meter). pH was measured using a digital pH meter (wissenschaftlich-TechnischeWerkstätten GmbH WTW/pH meter in lab pH720-Germany). The performance of the electrode was investigated by measuring the potential of MBV.HCl and Metronidazole benzoate solutions at room temperature with a concentrations range from10^{-6} to 10^{-1}M. While stirring, the potential reading was noted at equilibrium for each solution. The calibration curves obtained by plotted the response against logarithmic function of mebeverine and Metronidazole benzoate concentration.

Synthesis of the imprinted polymer (MIP)

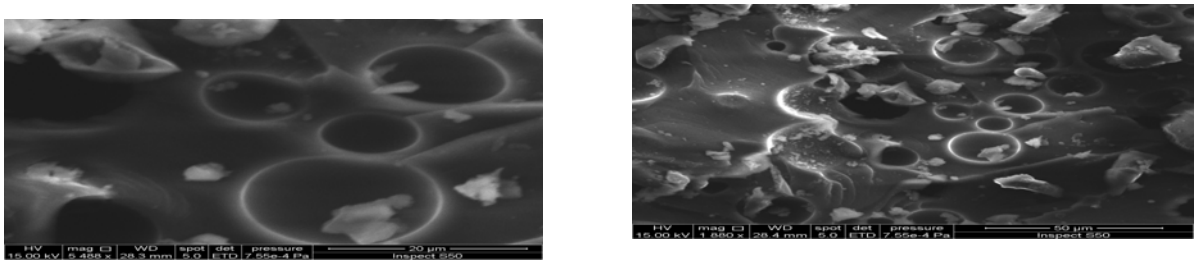
In a 50 mL screw cap glass test tube(50mL), MIPs for (Mebeverine hydrochloride) was produced by using a bulk polymerization method. The template (MBV) 0.5mmol (0.2330g) or 3.6mmol (1.7028) g was dissolved in a thick walled glass tube filled with chloroform (5 mL). A functional monomer either (2-Acrylamido-2-methyl-1-propane Sulphonic acid(AMPS) 3mmol (0.6217) g,

or (1-Vinylimidazole) 14mmol, cross-linker (pentaerythritol triacrylate (PETRA) or Divinylbanzene)73mmol and correspondingly initiator (BPO) 0.32 mmol (0.0775g) were then put in the tube to be mixed with the solution.
In an ultrasonic water bath for a period of 35 minutes, the nitrogen purged the mixture. After removing the glass tube from the ultrasonic water bath, during the nitrogen keeping flow, it has been sealed then put in 65°C waterbath to permit starting the reaction which continued 1 hr. MIP for (Metronidazole benzoate) was synthesized using a bulk polymerization.

The mold (MNZB) 0.5mmol (0.1377g) was dissolved in 10 mL of chloroform in a thick glass tube. A functional monomer either (2-Acrylamido-2-methyl-1-propane Sulphonic acid (AMPS) 3mmol (0.6217) g, or (1-Vinylimidazole) (VIZ) 3mmol, cross-linker (pentaerythritol triacrylate (PETRA)30mmol or (Divinylbanzene) (DVB) 30mmol, and initiator (BPO) 0.32 mmol (0.0775g) were then added to the above solution respectively. The polymer was prepared by using these compounds according to the same procedure used in preparing the MBV polymers. The two templates were removed by repeated washing with the MIPs successively with 100 mL portions of 30% (v/v) acetic acid /methanol solution by using soxhlet extraction. The polymer was dried at (35-45) ºC for (24-48) hours, the polymers were then crushed and grounded using mortar and pestle and sieved to particles size 125µm (using 100 mesh sieve); After the polymer was completely dried at ambient temperature, it was used as an active material in the selective sensor membrane. The non-printed polymer was (NIP) was made at the same way but without the template drug.

Prepare PVC membrane

To prepare specific PVC membrane, high molecular weight PVC (0.17g) mixed together with the MIP (0.02g) and the plasticizer (0.40g) until the solution become homogenized, then THF (2-3 mL) was added and stirred. The solution was transferred to glass vessel based on glass board with 5cm dia. circular section to let this mixture evaporate for 24 hours. A glass tube contains a silver wire painted with silver chloride and filled with 0.1 M standard solution of Mebeverine hydrochloride or Metronidazole benzoate was connected to one end of the Tygon tube tightly while the second end of the tube was attached to 10mm dia. circular disk of the PVC membrane by using a concentrated PVC/THF solution as a glue in purpose of producing the electrode.
A scanning electron microscopy (SEM) was used for primary evaluation of the MIP particles. The morphology of MIP and NIP membranes for Metronidazole benzoate before and after washing is shown by electron microscope in figure (4) porous on the surface figure (4a) about 20 µm may indicate the binding sides to the polymer. Figure (4b) shows clear holes about 50 µm in sizes have been obtained and were removed by soxhlet extraction.



a b

Figure (4): SEM photograph of the surface of MIP, a) after washing b) before washing

Potential measurements

At room temperature (20°C) with continuous magnetic stirring of the test solution (50 mL) which was put in double walled glass cell, all measurements were done. The electrodes performance was studied by measuring the potential of standard solutions for drugs produced with a concentration ranged from 10^{-6} to 10^{-1} M by serial dilution. The response time, slope, detection limit and operative life were calculated from the calibration curve. Depending on the IUPAC recommendations data, the electrochemical performance of the two suggested sensors was measured.

Preparation of pharmaceutical samples.

Three types of Tablets were used to determine the concentration of Mebeverine hydrochloride, and three types of capsules were used to determined Metronidazole benzoate.

1- Egypt-(Asia), B.P(135 mg Dospataline), Syria-(Eipico) B.P(135mg) (Colospasmin) Tablets, Holand-(Abbott) B.P (135mg) (Duspatalin) capsules. (0.3617g) of these Tablets were grinded and dissolved in Deionized water and completed in volumetric flask to (100ml).

2- France-(Framar Lyon): B.P(500) mg (Flagyl) Tablets, U.A.E-(Julphar) B.p(500) mg (Negazole Tablets, India-(MICRO LABS LIMITED) B.P(500mg) (Metronidazole) capsules were grinded(0.0275g) and dissolved in 1N(HCl) and completed in volumetric flask to (100ml).

Results and discussion

Influence of membrane composition

Liquid electrode membranes

The working ranges of liquid electrode membranes, Nernstian response and their slopes have been studied depending on MIP liquid electrodes which is made of the monomers AMPS and VIZ combined in a PVC matrix plus the two plasticizers DBS and TEHP. The inner solution was 0.1M aqueous standard solution of drug. (AMPS) and (VIZ) were used for the synthesis of MIPs and NIPs. The findings show that the two monomers can be used for producing effective MIPs for MBV and MNZB in spite of that the acid-base properties of them are different. The plasticizer is an essential component of the sensing membrane that acts as a solvent for the numerous components and identify the flexibility of the analyte in it. The used DBS and TEHP are suited for the production of MIP-based MBV and MNZB electrodes. Table (1) present the parameters of the fabricated and tested electrodes, four membranes of the different compositions which were prepared using four different plasticizers with different viscosities, Dibutylsebacate

(DBS) (ν=11.0042cSt) and tris(-2-Ethyl hexyl) phosphate (TEPH)(ν=8.015 cSt). The results of electrode specification were obtained from the calibration curves that listed in table (1) It is clear that the liquid electrodes have slopes 19.62-57.36 mV/decade and linear dynamic ranges between 1.2×10^{-6}- 2.0×10^{-5} M. The prepared liquid electrodes have 1 min. response time particularly at high concentrations which is short time. The best results among the tested electrodes is gotten by the liquid electrodes built on TEHP plasticizer as shown in table (1), thus, this liquid was used to identify the two drugs in pharmaceutical samples.

Table (1): Parameter of MBV-MIP electrodes based on different plasticizers

Electrode No.	Membrane composition	Parameter				
		Slope mV/decade	Correlation Coefficient(r)	Linearity range/ M	Detection limit/ M	Life time / day
IB	MBV-MIP +DBS	19.62	0.9999	$1\times(10^{-5}\text{-}10^{-2})$	4×10^{-6}	50
IIB	MBV-MIP +TEHP	29. 10	0.9987	$1\times(10^{-5}\text{-}10^{-1})$	3×10^{-6}	40
IT	MNZB-MIP + DBS	52.23	0.9984	$1\times(10^{-6}\text{-}10^{-1})$	2×10^{-5}	50
IIT	MNZB-MIP+TEHP	57.36	0.9997	$1\times(10^{-6}\text{-}10^{-1})$	$1.2\text{x}10^{-6}$	40

pH influence

pH effect on the 4 electrodes potential values was investigated for pH ranged from 1.5 to 12 and adjusting the pH by putting drops of 0.1 N HCl and 0.1 M NaOH to the aqueous solutions of the drugs then the obtained potentials at each value were noted.

For three concentrations 1×10^{-2}, 1×10^{-3} and 1×10^{-4} to M of standard solutions of drugs, the pH effect on the electrode potential was recorded. The obtained results are shown in table (2) and the typical plot of electrode potential versus pH for electrode IIB and IIT are shown in figure (5).

Table (2): Working pH ranges for MBV-MIP electrodes

Electrode No.	Membrane composition	pH range		
		$1\text{x}10^{-2}$	$1\text{x}10^{-3}$	$1\text{x}10^{-4}$
IB	MBV-MIP +DBS	1.5-11	1.5-10	1.5-9
IIB	MBV-MIP + TEHP	1.5-7.5	1.5-8.5	1.5-8.5
IT	MNZB-MIP + DBS	1.5-12	1.5-12	1.5-12
IIT	MNZB-MIP + TEHP	1.5-12	1.5-12	1.5-12

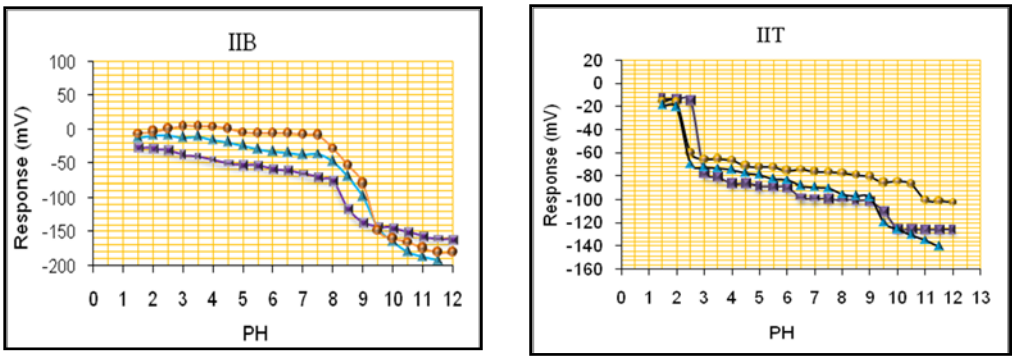


Figure (5): Typical plot of electrode response versus pH of electrode IIB and IIT at different concentrations

Response time and life time

The response time for all MBV.MIP and MZNB.MIP electrodes was obtained from the dynamic potential response at concentration range between $1 \times 10^{-6} - 1 \times 10^{-1}$ M by measuring the time required to reach 95 % equilibrium potential. The results indicate that the response time of the electrodes was approximately 15seconds for the solution of mebeverine at high concentration 10^{-1} M and about 46 seconds at low concentration 10^{-6} M compared with appearance 30 seconds for the solution of metronidazole benzoate at high concentration 10^{-1} M and about 55 seconds at low concentration 10^{-6}M. The electrode lifetime was obtained by measuring the slope periodically from calibration curves for MBV.MIP and MZNB.MIP during 40-50 days. See tables (3) and (4).

Table (3): Response time of Mebeverine hydrochloride electrode

Membrane composition	Concentration (M)	Potential (mV) at t/100	Time (s) at 95%	Time (s) at 100%
MIP+ DBS (IB)	10^{-1}	-2.4	5	5.3
	10^{-2}	2.7	4.8	5.1
	10^{-3}	-3.6	15	15.8
	10^{-4}	-6.8	55.9	58.8
	10^{-5}	-3.9	57	60.0
	10^{-6}	6	57	60.0
MIP+ TEHP (IIB)	10^{-1}	5.6	32	33.7
	10^{-2}	-2.1	34	35.8
	10^{-3}	-3.2	47.0	49.5
	10^{-4}	0.6	50	52.6
	10^{-5}	1.3	51	53.7
	10^{-6}	-2.8	59	62.1

Table (4): Response time of Metronidazole benzoate electrode

Membrane composition	Concentration (M)	Potential (mV) at t/100	Time (s) at 95%	Time (s) at 100%
MIP + DBS (IT)	10^{-1}	-4.6	5.2	5.5
	10^{-2}	-8	21	22.1
	10^{-3}	-8.1	44	45.8
	10^{-4}	-16.2	55.8	58.7
	10^{-5}	-9.1	57	60.0
	10^{-6}	-13.8	59	62.1
MIP + TEHP (IIT)	10^{-1}	-0.4	15.2	16.0
	10^{-2}	-4.2	15.3	16.1
	10^{-3}	-10	29	30.5
	10^{-4}	-22.7	34	35.8
	10^{-5}	26.1	38	40.0
	10^{-6}	-5.4	46	48.4

Selectivity coefficient

Separate solution method (SSM) was used to identify the selectivity coefficients of the potentiometric sensor toward various types. In the SSM, the potential of a cell comprising a working electrode and a reference electrode are measured for two separate solutions; first solution contains the drug ions (E1) while the second solution contains the potential of

interfering ions (E2) where S is the calibration graph slope. Coefficient selectivity was calculated using the following equation:

(Log Kpot =$(E_2-E_1)\ Z_1F/2.303RT + (1-Z_1/Z_2)\log a_{1)}$

Coefficient selectivity of the electrodes IIB and IIT were studied toward several different substances; inorganic ions (Li^{+1},Ca^{2+} and Fe^{+3}) and amino acids (proline,Alanine,Serine and Glycine). Plot of coefficient selectivity versus log concentration of Mebeverine was measured at concentrations range from 10^{-1} to 10^{-6}M using electrode IIB is shown in figure (7a) and (7b) As we noticed that all species, cations and amino acids at various concentrations show no interference on electrode response. The values of coefficients selectivity at two mebeverine concentrations 10^{-3} M and 10^{-4} M using electrodes IIB and IIT are listed in table (5). The results in table (5) showed that all interfering species have no effect on electrode response, for example the coefficient selectivity range was from 2.223×10^{-2} at low concentration of Mebeverine to 4.273×10^{-7} at high concentration of mebeverine and for electrode IIB the selectivity coefficients range was from 1.677×10^{-3} to $4.563x\times10^{-6}$.

Table (5): Result of selectivity coefficients using separate solution method for some interfering species (cations and amino acids)

Con. (M)	Concentrations of Mebeverine.HCL (M): Concentrations of interference ions (M)						
	Interfering ions			Amino acids			
	Li^+	Ca^{2+}	Fe^{3+}	Alanin	Glysin	proline	Serine
	$K_{A,B}$	$K_{A,B}$	$K_{A,B}$	$K_{A,B}$	$K_{A,B}$	$K_{A,B}$	$K_{A,B}$
10^{-6}	2.30×10^{-1}	1.20×10^{-4}	1.38×10^{-3}	1.41×10^{-2}	7.42×10^{-4}	1.50×10^{-3}	4.02×10^{-3}
10^{-5}	9.0110^{-2}	1.15×10^{-4}	6.66×10^{-3}	1.01×10^{-1}	7.94×10^{-3}	1.56×10^{-2}	3.69×10^{-2}
10^{-4}	4.06×10^{-2}	9.69×10^{-5}	3.47×10^{-2}	1.84×10^{-1}	1.84×10^{-2}	3.74×10^{-2}	8.21×10^{-2}
10^{-3}	9.69×10^{-3}	4.32×10^{-5}	1.38×10^{-1}	7.30×10^{-2}	9.49×10^{-4}	2.89×10^{-3}	6.98×10^{-3}
10^{-2}	4.41×10^{-3}	2.70×10^{-5}	3.83×10^{-1}	5.91×10^{-2}	1.32×10^{-5}	4.33×10^{-5}	1.50×10^{-4}
10^{-1}	1.48310^{-3}	3.01×10^{-5}	5.57×10^{-1}	3.35×10^{-1}	4.94×10^{-6}	1.59×10^{-5}	5.17×10^{-5}
Conc. (M)	Interfering ions			Amino acids			
	Li^+	Ca^{2+}	Fe^{3+}	Alanin	Glysin	proline	serine
	$K_{A,B}$	$K_{A,B}$	$K_{A,B}$	$K_{A,B}$	$K_{A,B}$	$K_{A,B}$	$K_{A,B}$
10^{-6}	9.76×10^{-3}	1.94×10^{-6}	6.83×10^{-8}	9.76×10^{-3}	2.04×10^{-3}	2.31×10^{-2}	3.88×10^{-3}
10^{-5}	2.06×10^{-2}	1.14×10^{-5}	4.59×10^{-7}	2.06×10^{-2}	3.54×10^{-3}	1.01×10^{-2}	2.17×10^{-3}
10^{-4}	8.10×10^{-2}	1.40×10^{-4}	4.86×10^{-6}	8.10×10^{-2}	1.55×10^{-2}	1.89×10^{-2}	2.33×10^{-3}
10^{-3}	1.98×10^{-1}	8.40×10^{-4}	3.83×10^{-5}	$1.98\times^{-01}$	5.30×10^{-2}	1.93×10^{-2}	7.01×10^{-3}
10^{-2}	8.02×10^{-1}	4.46×10^{-3}	4.43×10^{-4}	$8.02\times^{-01}$	1.34×10^{-1}	3.03×10^{-2}	4.15×10^{-3}
10^{-1}	8.95×10^{-1}	1.62×10^{-2}	2.65×10^{-03}	$8.95\times^{-01}$	7.18×10^{-1}	5.95×10^{-2}	1.45×10^{-2}

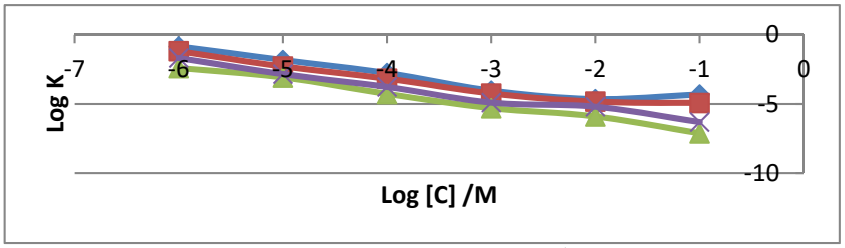


Figure (6): Variation of selectivity coefficient Log $K^{pot}_{A,B}$ with concentration at ($a_A = a_B$) using electrode IIB.(◊ - Alanin, □ – Glysin, X – Serine, Δ – Proline)

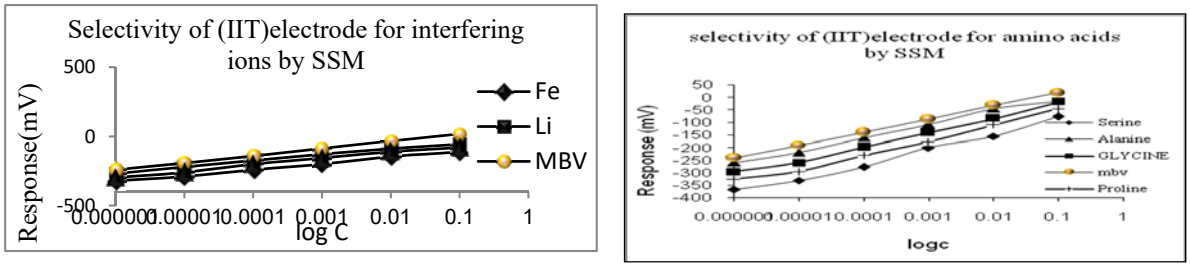


Figure (7): Selectivity of (IIT) electrode for interfering ions and amino acids by SSM

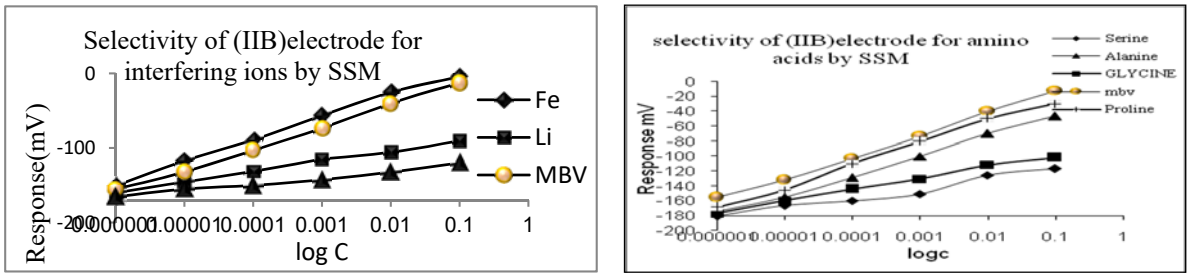


Figure (8): Selectivity of (IIB) electrode for interfering ions and amino acids by SSM.

Quantitative analysis

The accuracy of electrodes IIB and IIT was measured by determining mebeverine in synthetic solutions of 10^{-3} and 10^{-4} M using standard addition method. Excellent results of %recovery were obtained in the range 97.95 to 102.73. A typical plot for membrane IIB at concentration of synthetic solution 10^{-3} M is shown in figures (9) and (10) and the standard solution added was 0.1 M.

Direct method and standard addition method were applied for the determination mebeverine in commercial pharmaceutical (Asia-duspataline 135 mg, Epico-colospasmia135 mg and Abbott-duspataline 135 mg) obtained from local storages using membrane IVB based on TEHP plasticizer. The values of the % recovery tables (6) and (7) agree with the value given in British Phamacopoeia [6]. There is no interference of all species on electrode response, therefore, the values of recovery obtained by standard addition method agree with the results of direct method.

Table (6): Results of recovery and standard deviation of commercial drugs obtained by using membrane IIB.

Pharmaceutical Drug	Potentiometric methods	Concentration Prepared/ M	Concentration Found/ M	%Rec.	%RE	%RSD	F-experimental	F theoretical
Asia-duspataline 135 mg	Direct method	$1.0x10^{-3}$	$0.10448 x10^{-3}$	104.48	4.48	0.45	14.2	19.2
	SAM		$9.9851 x10^{-3}$	99.85	-0.15	-0.10	15.4	
	Direct method	$1.0x10^{-4}$	0.9495×10^{-4}	94.95	-5.05	1.21	5.3	19.2
	SAM		1.0472×10^{-4}	104.72	4.72	-0.22	7.4	
Epico-colospasmia 135 mg	Direct method	$1.0x10^{-3}$	0.1056×10^{-3}	105.60	5.60	1.20	13.2	19.2
	SAM		1.0515×10^{-3}	105.15	5.15	-0.07	12.5	
	Direct method	$1.0x10^{-4}$	0.10580×10^{-4}	105.79	5.79	0.79	10.6	19.2
	SAM		0.9356×10^{-4}	99.36	-0.64	-0.16	15.7	
Abbott-duspataline 135 mg	Direct method	$1.0x10^{-3}$	0.9938×10^{-3}	99.38	-0.62	0.79	15.4	19.2
	SAM		1.0496×10^{-3}	104.58	4.58	-0.13	10.9	
	Direct method	$1.0x10^{-4}$	$0.1052 x10^{-4}$	105.24	5.24	0.45	13.5	19.2
	SAM		$1.0186 x10^{-4}$	101.86	1.86	0.96	18.2	

Table (7): Results of recovery and standard deviation of commercial drugs obtained by using membrane IIT.

Pharmaceutical Drug	Potentiometric methods	Concentration Prepared/ M	Concentration Found/ M	%Rec.	%RE	%RSD	F-experimental	F theoretical
Asia-duspataline 135 mg	Direct method	$1.0x10^{-3}$	1.0302×10^{-3}	103.02	3.02	4.70	9.5	19.2
	SAM		1.0491×10^{-3}	104.91	4.91	-0.52	11.3	
	Direct method	$1.0x10^{-4}$	1.0337×10^{-4}	103.37	3.37	3.58	11.1	19.2
	SAM		0.97870×10^{-4}	97.87	-2.13	-0.80	15.4	
Epico-colospasmia 135 mg	Direct method	$1.0x10^{-3}$	0.10392×10^{-3}	103.92	3.92	10.13	12.6	19.2
	SAM		1.0495×10^{-3}	104.95	4.95	-0.99	14.2	
	Direct method	$1.0x10^{-4}$	1.0200×10^{-4}	102.00	2.00	3.22	8.8	19.2
	SAM		0.98115×10^{-4}	98.12	-1.88	-1.10	6.7	
Abbott-duspataline 135 mg	Direct method	$1.0x10^{-3}$	0.97724×10^{-4}	97.72	-2.28	5.11	9.5	19.2
	SAM		0.97110×10^{-3}	97.11	-2.89	-4.81	7.5	
	Direct method	$1.0x10^{-4}$	1.0487×10^{-4}	104.87	4.87	1.77	-2.17	19.2
	SAM		1.2622×10^{-4}	126.22	26.22	-0.46	4.42	

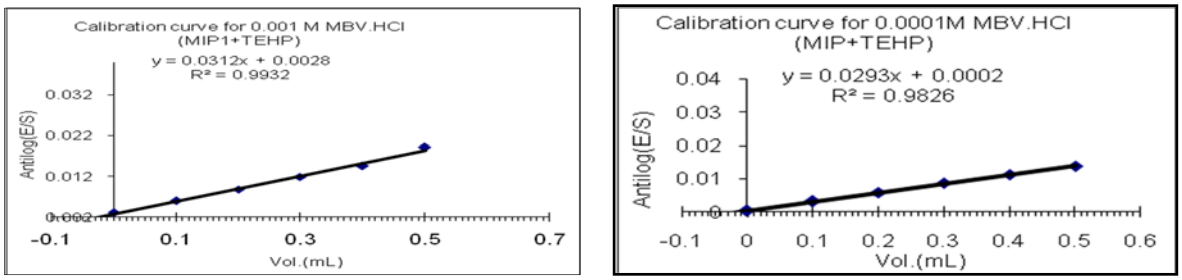


Figure (9): Variation of antilog (E/S) of synthetic solution of 10^{-3},10^{-4} M versus mL of standard MBV added using electrode IIB.

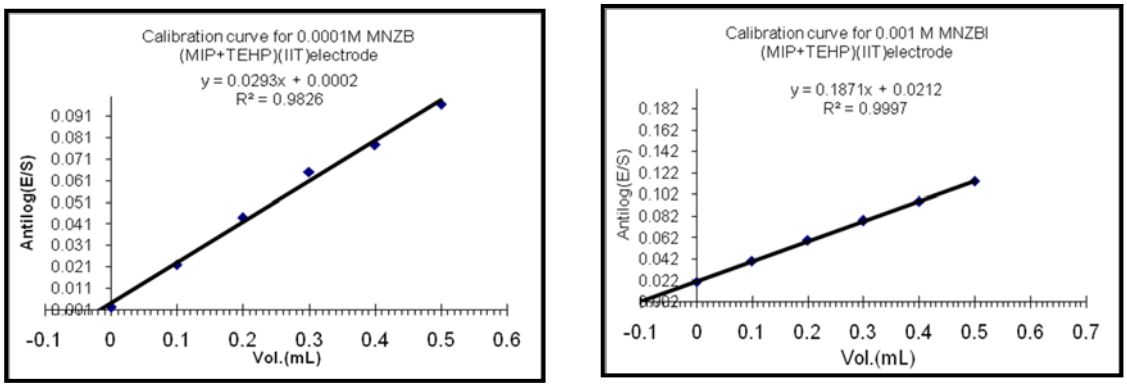


Figure (10): Variation of antilog (E/S) of synthetic solution of 10^{-3},10^{-4} M versus of standard MNZB added using electrode (IIT).

Conclusion

The construct ion of molecularly imprinted electrodes sensors (MIP) using mebeverine and Metronidazole benzoate as a template and 2-Acrylamido2-methyl-1-propane sulphonic acid(AMPS) as monomer in different plasticizers. Results of MIP that show high sensitivity, reasonable selectivity, fast static response, long-term stability and applicability over a wide pH range were obtained by using electrode based on TEHP plasticizer. Good results of recoveries were obtained for the determination of Mebeverine and Metronidazole benzoate in the commercial Tablets in comparison with the British Pharmacopoeia.

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