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RESEARCH ARTICLE

Synthesis new Trifluoperazine Selective Liquid Electrodes Depending on Molecularly Imprinted Polymers Based on PVC Membrane for Determination of Trifluoperazine from Pharmaceutical Samples

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Abstract

Liquid electrodes of polymers imprinted with Trifluoperazine were synthesized based on Mechanics polymerization of precipitation. The molecularly imprinted polymer (MIP) and non-imprinted polymers (NIP) It was manufactured using (TFP) as a template. In polymerization process, 2-Hydroxy ethyl meth acrylate (2-HEMA) and 2-Vinyl Pyridine (2-VP) were used as monomers. Divinylbanzene (DVB) was used as cross-linkers and benzoyl peroxide (BPO) as an initiator. The molecularly imprinted membranes and the molecularly non-imprinted membranes were synthesized utilize DibutylSebacate (DBS) and Nitro benzene (NB) as plasticizers in PVC matrix. Detection limit and Slopes of the liquid electrodes are ranged at (3×10^{-6}– 8×10^{-6}) M and (21.83– 23.03) mV/decade, respectively. Response time was 60 seconds. The electrodes were filled with liquid of 10^{-1} M standard solution of drug and observed stable response for a pH ranged from 1.5 to 12 and with good selectivity for more than several types. The new synthesis electrodes were successfully used for the analyte estimated in preparation pharmaceutical sample without any time consuming pretreatment steps.

Keywords: *Molecularly imprinted electrodes; Trifluoperazine; Potentiometric method; (2-HEMA); (2-VP) monomers*

Introduction

Trifluoperazine, sold under a number of brand names, is a typical antipsychotic primarily used to treat schizophrenia. It may also be used short term in those with generalized anxiety disorder but is less preferred to benzodiazepines [1]. It is of the phenothiazine chemical class.

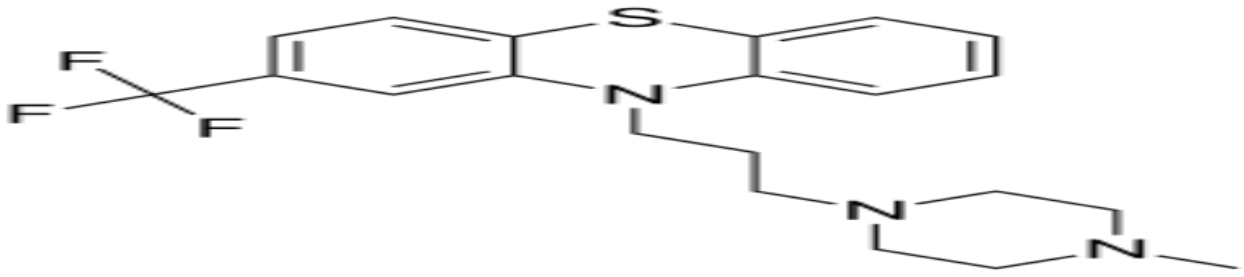


Figure 1: structure Trifluoperazine, (TFP)

Polymers are molecularly imprinted (MIPS), generally acting as synthetic antibody imitators [2], the candidates seemed very promising as highly selective adsorbents,[3] because inherent advantages such as reuse, physical, molecular specificity, stability and application in the harsh chemical media [4].MIPs Mainly on polymerization of functional monomers in the presence of a template molecule. The mold is filtered out leaving behind the cavities that are embedded in the shape, size and functionality of the mold. In Recently years, technology of MIP has develop to a value integral idea for biological activity With the possibility of an increase in the application of

analytical chemistry, which show a different and rapid methods for synthesis Polymer with a specific molecule activity Characteristics with applications ranging from purification of the mixture to the racemic, to catalytic control and chemical sensing of complex chemical reactions [5]. It was determination some drugs such as ibuprofen [6] and warfarin sodium [7] based on molecularly imprinted polymer method. In this study imprinted polymer electrodes were prepared based on Trifluoperazine as a template in PVC matrix membrane and electrodes specifications were studied.

Experimental

Chemicals

Trifluoperazine was obtained from the State Company of Drug Industries and Medical Appliances (IRAQ-SDI –Samara, Ajanta Pharma, and India). The Commercial Trifloberazine tablets obtained from local stores is Salabid1 mg and Trifloberazine1 mg .Nitrobenzene (NB) and Di-butyl sebacate (DBS) as well as metal salts were sold from Sigma-Aldrich and were utilized as they were got. Pentaerythritoltriacrylate (PETRA) (99 %), (2-Acrylamido-2-methyl-1-propane sulphonic acid (AMPS) (99%), or (1-Vinylimidazole) (99%), (pentaerythritoltriacrylate (PETRA) or Divinylbanzene) and benzoyl peroxide (BPO) (78%) were purchased from Sigma-Aldrich. The chemicals used in the search were possesses high purity does not need to purify.

Apparatus

Voltage measurements were also carried out with the digital voltmeter (HANA pH 211 instrument Microprocessor pH meter). Measurements were made of pH with a digital pH meter (wissenschaftlich-Technische Werkstätten GmbH WTW/pH meter in lab pH720-Germany), UV-Visible spectrophotometer double-beam model (UV-1800 PC) SHIMADZ (Japan), interfaced with computer via a SHIMADZU UV probe data system program (Version 1.10), using 1.00cm quartz cells, Infrared spectrophotometer SHIMADZU, FTIR-8000 (Japan), Scanning Electron Microscopy (SEM) [JSM-6390A] (Tokyo, Japan) and sensitive balance (Electronic balance ACS120-4 Kern &Sohn GmbH, Germany. The performance of the electrode was investigated by measuring the potential of Trifloberazine solutions at room temperature with a concentrations range from1×10-1 to 5×10-6 M. For the accuracy the potential of solutions were measured after the arrival of the internal and external solution to the equilibrium, then the potential recorded.

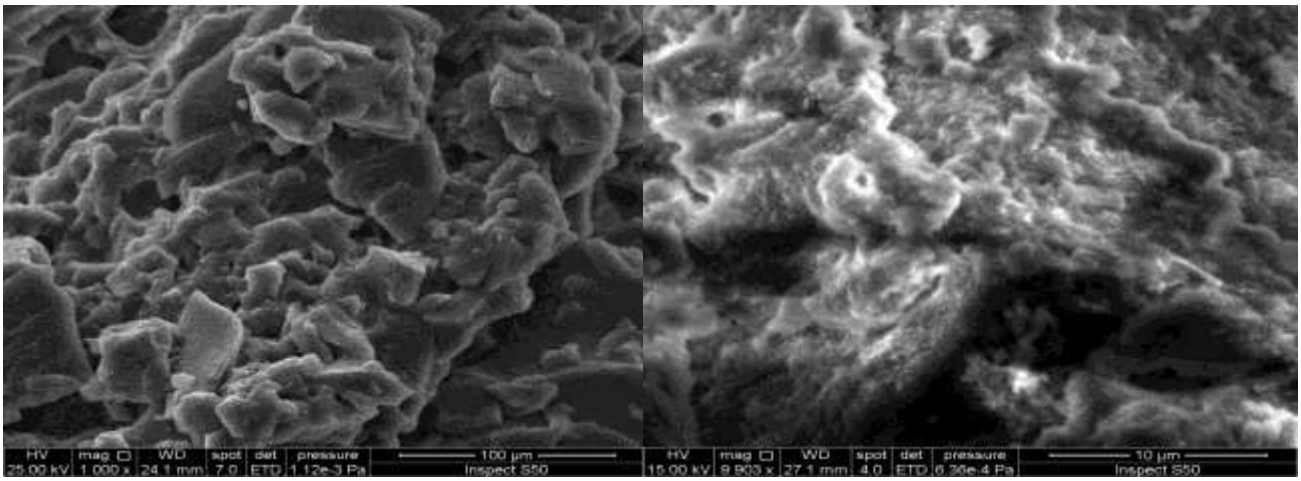
Synthesis of the imprinted polymer (MIP)

Bulk polymerization method was used for preparation of MIP. The template (TFP) of 0.5mmol was dissolved in a thick walled glass tube (50 mL capacity) filled with 10 mL chloroform. Two monomers were used for preparation of MIP, 2 mmole of 2 –vinyl pyridine (2V-P) with 10 mmole Divinyl benzene (DVB) as a cross-linker, the second MIP based on 4.6mmol of 2-hydroxy ethyl meth acrylate (2-HEMA) as a monomer with 9.99 mmol Divinyl banzene as cross-linker. The initiator of 0.2 mmole BPO was used. The solution was mixed in ultrasonic water bath for a period of 45 minutes [8], during this time the nitrogen gas was purged the mixture [9].

After 45 minutes seal the tube and put the tube in 65°C water bath to permit starting the reaction which continued for 2 day. The templates were Deleting by frequent washing of MIPS successively with 100 ml parts of 30% (v/v) acetic acid /methanol solution by using soxhletextraction [10]. The polymer has been dried at (35-45) °C for (24-48) hours, The polymers were then crushed and grounded using mortar and pestle and sieved to particles size 125 µm (using 100 mesh sieve); After the polymer dried completely at room temperature, it was used as an active material in the selective sensing membrane [11].The non-printed polymer NIP was made at the same way but without the template drug.

To prepare specific PVC membrane, high molecular weight PVC (0.17g) mixed together with the MIP (0.036g) and the plasticizer (0.4g) until the solution become homogenized, and then add THF (5-6 mL) and stirred. The solution was transferred to glass vessel based on glass board with 5cm. circular section to let this mixture evaporate for 24 hours. A glass tube contain a silver wire painted with silver chloride and filled with 0.1 M standard solution of Trifluoperazine was connected to one end of the Tygon tube tightly while the second end of the tube was attached to 10 mm [12].

Circular disk of the PVC membrane by using a concentrated PVC/THF solution as a glue in purpose of producing the electrode. For the sake of clarity of the morphology and design of the particles and were used scanning electron microscope (SEM) .The morphology of MIP and NIP membranes for Trifluoperazine before and after washing is showed by electron microscope in Figure 2. A porous on the surface (figure 2a) about 20 µm may indicate the binding sides to the polymer. Figure 2b shows clear holes about 50 µm in sizes have been obtained and which were removed by soxhlet extraction.



a **b**

Figure2: SEM photograph of the surface of MIP, a) after washing b) before washing

Potential Measurements

Measurements were carried out in a double cell on 50 mL glass walls, magnetic stirring was used for obtain a homogeneous solution and under laboratory. The efficacy of the electrodes was scrutinized by measuring the potential of standard solutions for drugs prepared with a concentration range of 1×10^{-1} to 5×10^{-6} M by many dilution. The slope, detection limit, and response time operative life were calculated from the calibration curve.

Preparation of Pharmaceutical Samples

Two types of tablets were used to determine the concentration of Trifluoperazine (IRAQ-SDI –Samara, Ajanta Pharma, and India). The Commercial Trifloberazine tablets obtained from local stores is Salabid1 mg and Trifloberazine1 mg. tablets were grinded (0.0275g) and dissolved in 1M (HCl) and completed in volumetric flask to (100ml).

Results and Discussion

Characterization

The FTIR spectra of the drugs, MIP based on (2-Vinyl Pyrdine) as basic functional monomer (before and after the removal of template) and their NIPs are shown in Figures (3-5) for (TFP) drug. Table 1 summarized the main peaks that appeared in these figures.

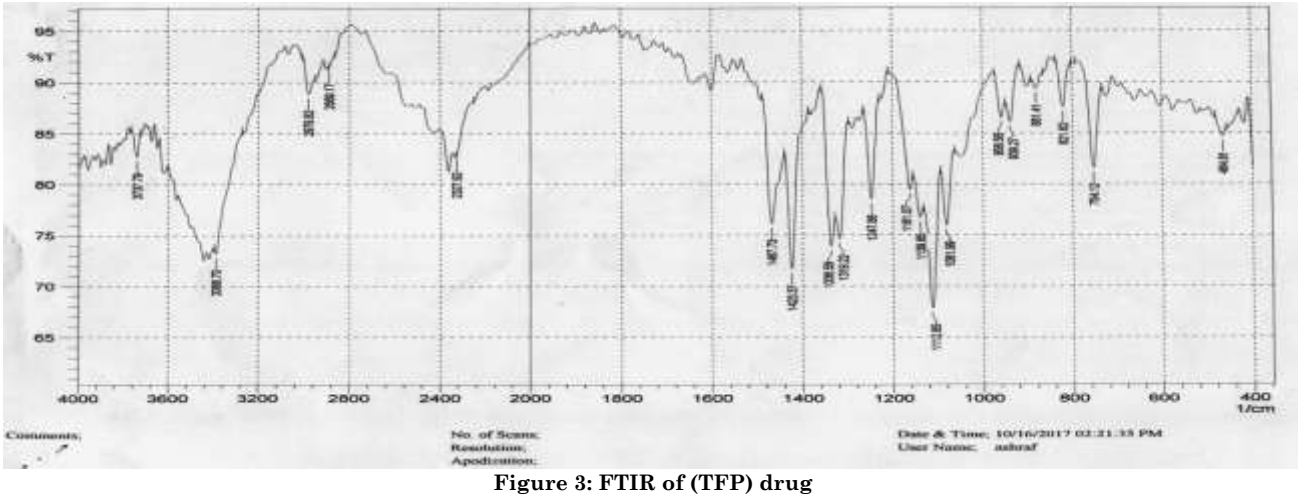


Figure 3: FTIR of (TFP) drug

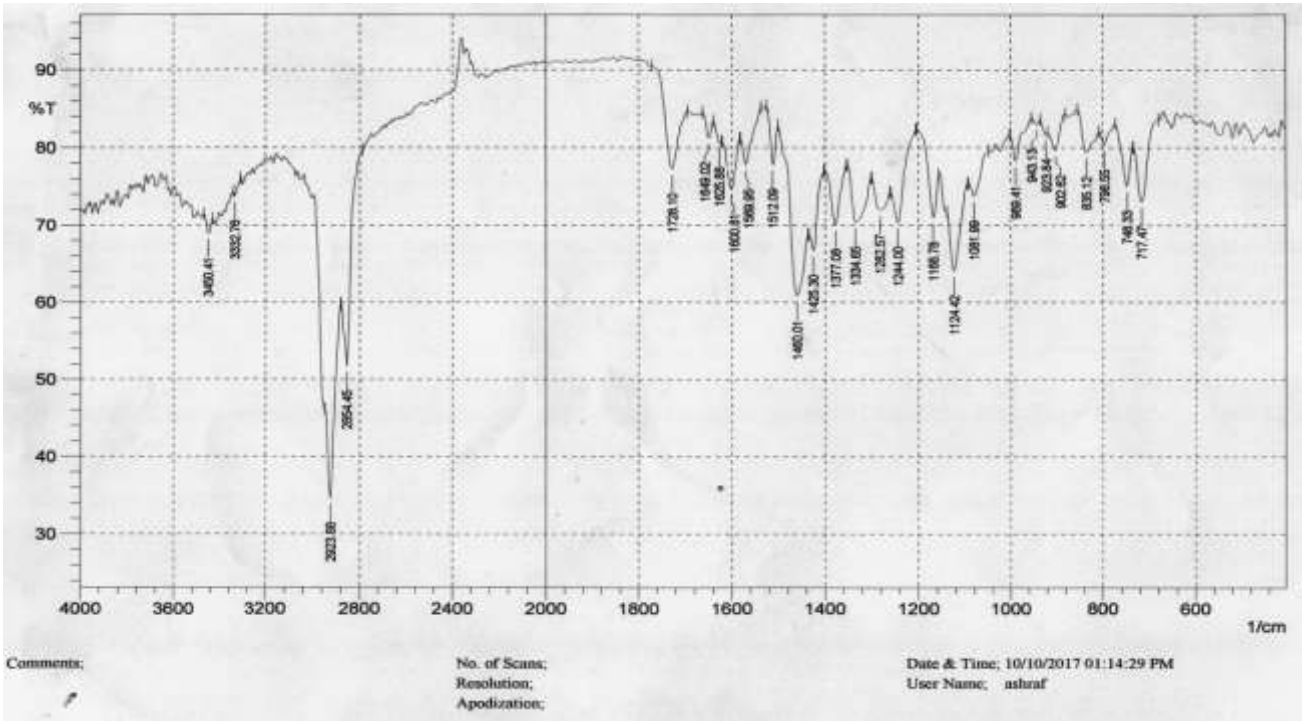


Figure4: FTIR of TFP-MIP (2-VP) before the removal of (TFP)

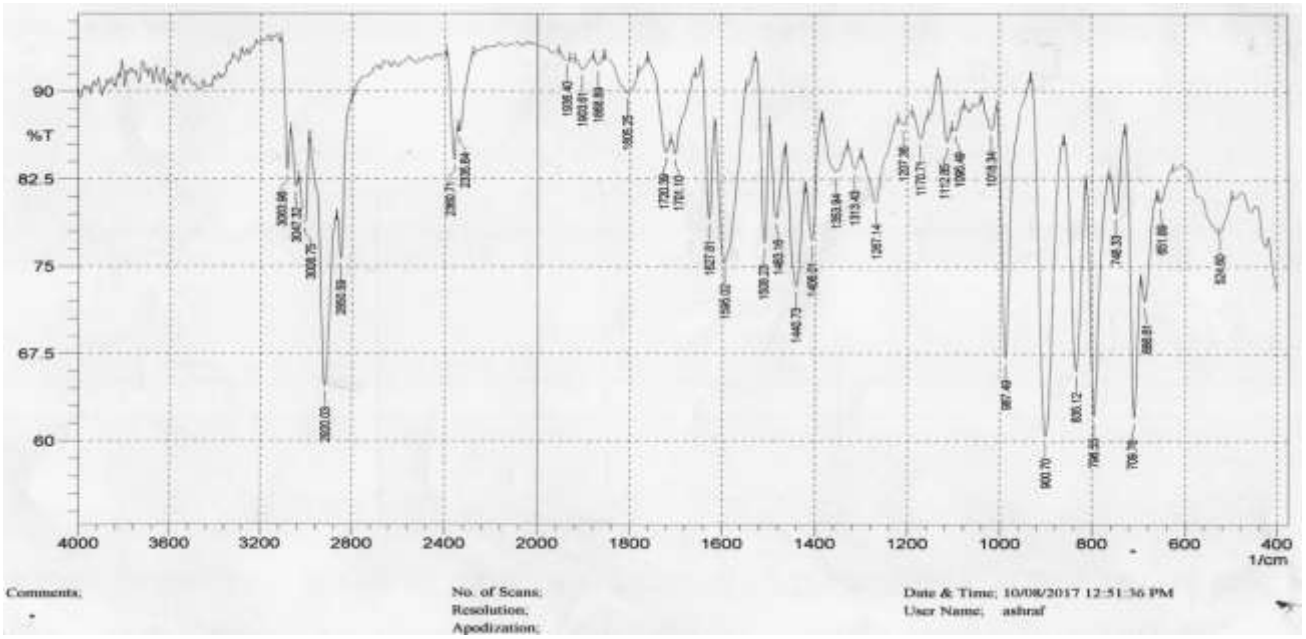


Figure5: FTIR of TFP-MIP (2-VP) after the removal of (TFP)

Table 1: The most identified peaks of FT-IR spectra for TFP-imprinted polymer using (2-VP) as a functional monomer

	Functional Group	Drug(TFP)	TFP-MIP(2-VP) before Template removal	TFP-MIP(2-VP) after Template removal
1	N-H str. (cm^{-1})	3450	----	----
2	C-F str.(cm-1)	1112	1124	----
3	C=C aromatic.(cm^{-1})	1600	1600	1595
4	C-H str.alphatic.(cm^{-1})	2923,2854	2979,2889	2920,2850
5	C=O str ester (cm^{-1})	1728	----	----
6	C=C olefiine	-----	1625	1627

The FTIR spectra for Drug , before , after show the significant band at 1625cm^{-1} (before) and 1627cm^{-1} (after) for C=C olefiine which not exsist in the Drug spectrum also the drug spectrum show strong band at 1112cm^{-1} for C-F band which not exsist in the third spectrum.

The FTIR spectra of the drug, MIP based on (2-HEMA) as acidic functional monomer (before and after the removal of template) are shown in figures (3.69) to (3.70) for (TFP) drug. Table (2) summarized the main peaks that appeared in these figures.

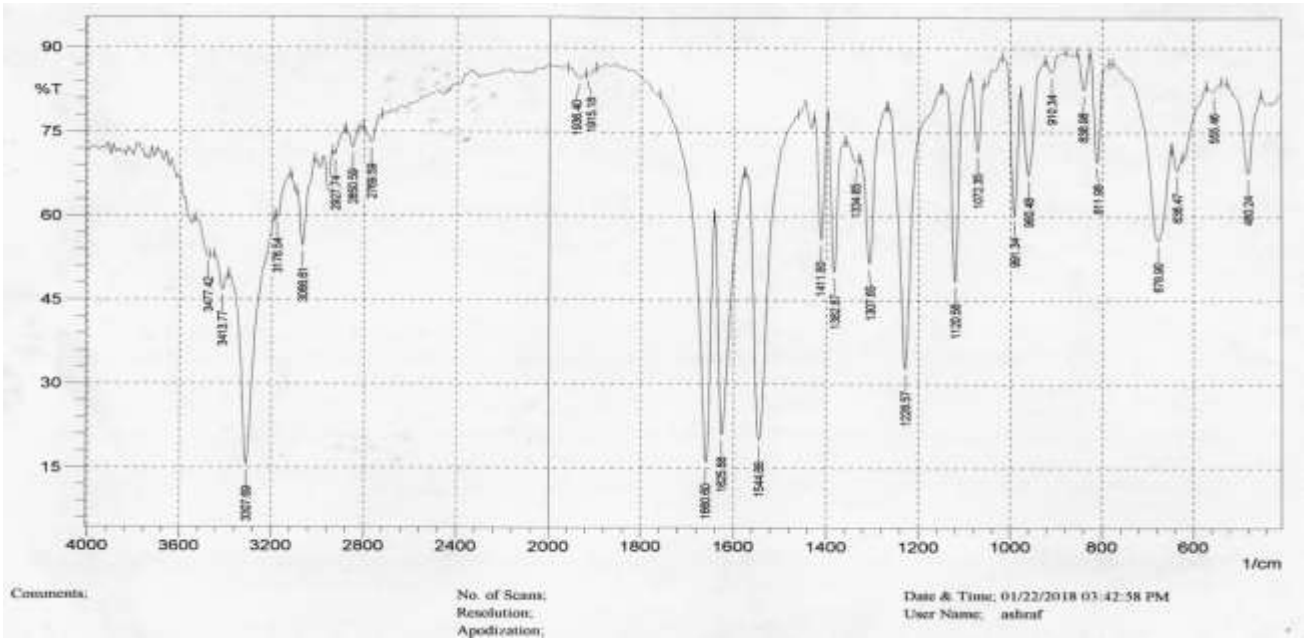


Figure6: FTIR of TFP-MIP (2-HEMA) before the removal of (TFP)

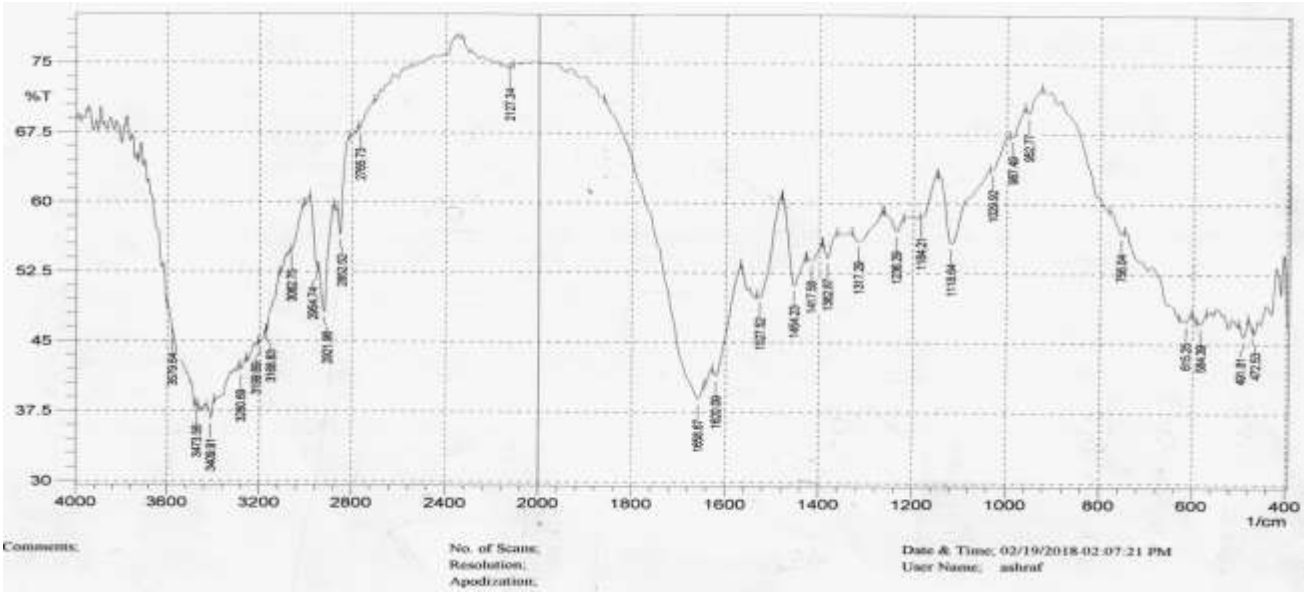


Figure7: FTIR of TFP-MIP (2-HEMA) after the removal of (TFP)

Table 2: The most identified peaks of FT-IR spectra for TFP-MIP using (2-HEMA) as a functional monomer

	Functional Group	Drug(TFP)	TFP-MIP(2-HEMA) before Template removal	TFP-MIP(2-HEMA) after Template removal
1	N-H str. (cm^{-1})	3400	3413	----
2	C-F str.(cm-1)	1081	1072	----
3	C=C aromatic.(cm^{-1})	1600	1544	----
4	C-H str.alphatic.(cm^{-1})	2983	2927,2850	2921,2852
5	C=O str ester (cm^{-1})	----	1660	1658
	O-H str(cm^{-1})	----	3307	3409
6	C=C olefiine	-----	1625	1620

The FTIR spectra of Drug , before , after the FTIR spectrum of drug show bands at 3400 cm^{-1} ,1600 cm^{-1} and 1081 cm^{-1} for N-H stretching alpha tic , C=C and C-F stretching .While the FTIR spectrum of (before) show bands at 1660cm^{-1} and 3307 cm^{-1} for extraction. C=O ester and O-H stretching. The FTIR spectrum (after) show the disappearance of N-H is stretching and C-F stretching which give good indication for the drug.

Liquid Membranes Electrode

MIP based liquid electrodes, their concentrations range and slopes response to Nernstian equation has been investigated.

The membranes of MIP made of the monomers 2-HEMA and 2-VP with a PVC template using two plasticizers DBS and NB. The internal solution was used 0.1M aqueous standard solution of drug for all liquid electrodes. Experimental results of synthesis of molecularly imprinted (MIP) and non-imprinted polymers (NIP) based on two monomers 2-HEMA and 2-VPIndicates that both monomers can be used for effective MIP setup for Trifluoperazine.

The plasticizer is an essential part of the sensing membrane which have important role as a solvent for the different components and specifies the analytical mobility in membrane. All of the plasticizer that are used, DBS and NB, are suitable for making of Trifluoperazine based electrodes MIP. Table 3 show the parameters of the fabricated and tested electrodes, Four membranes of the different compositions were prepared using two different plasticizers with different viscosities, dibutylsebacate (DBS) (v=11.0042cSt) and Nitro benzene (NB)(v = 2.030 cST). The results of electrode specification were obtained from the calibration curves that listed in Table 3.

The slopes of the electrodes ranged between 21.83-23.03 mV/decade and detection limit ranges between 3×10^{-6}- 8×10^{-6}M. In generally the preparation electrodes have a short response time (about 60 second) mostly at high concentrations. The values listed in table 3 also indicate the electrodes IT and IVT give the good results therefore, the liquid electrode were used to determine both drugs in pharmaceutical samples.

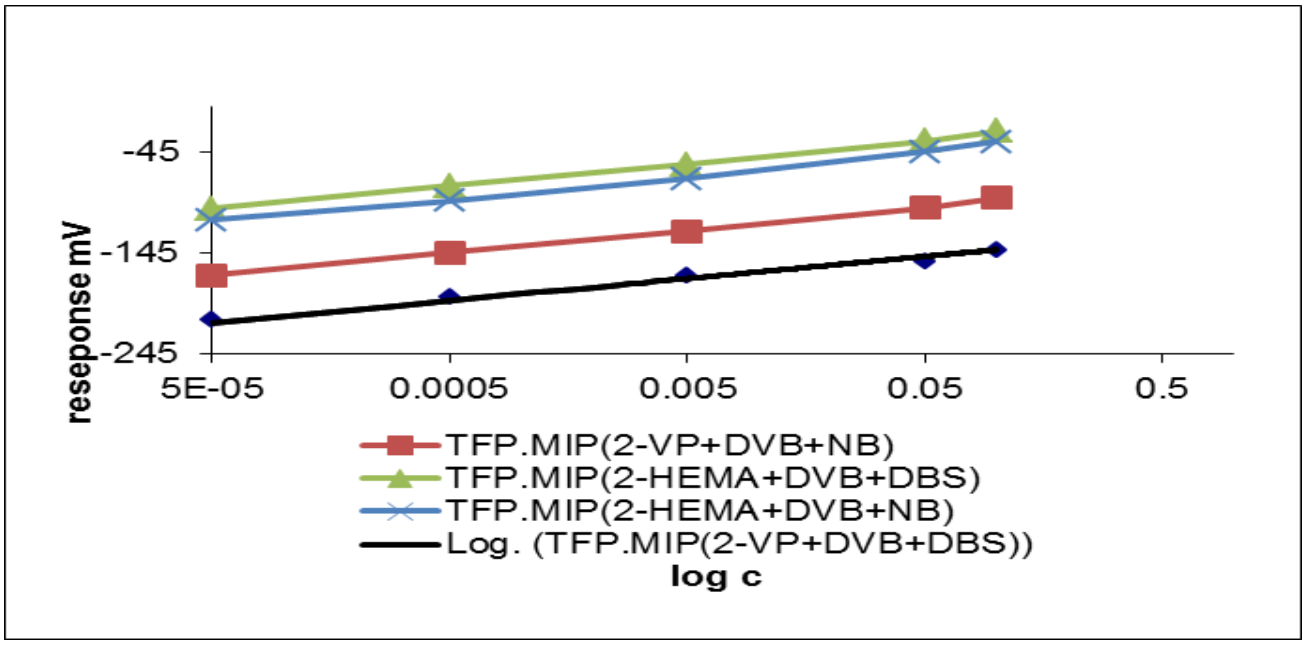


Figure8: Calibration curves of Trifluoperazine- selective electrodes: IB, IIB, IIIB, IVB

Table 3: Parameter of TFP-MIP electrodes based on different plasticizers

Electo de No.	Membrane Composition	Parameter				
		Slope (mV/dec.)	Detection limit (M)	Correlation coefficient	Linearity range (M)	Life time
IB	TFP –MIP1(2-VP +DVB+DBS)	21.83	$3x10^{-6}$	0.990	$4x10^{-5}$-$1x10^{-1}$	50
IIB	TFP-MIP1(2-VP +DVB+NB)	21.84	$7x10^{-6}$	0.996	$2x10^{-5}$-$1x10^{-1}$	45
IIIB	TFP-MIP2(2-HEMA+DVB+DBS)	21.84	$6x10^{-6}$	0.966	$4x10^{-5}$-$1x10^{-1}$	40
IVB	TFP-MIP2(2-HEMA+DVB+NB)	23.03	$8x10^{-6}$	0.966	$6x10^{-6}$-$1x10^{-1}$	45

Influence of PH

The effect of acidity on the values of potential was studied over pH range from 1.5 to 12 and adjusting the pH by adding drops of 0.1 M HCl and 0.1 M Na OH to the aqueous solutions of the drugs and the obtained potentials at each value were recorded. The effect of pH on the electrode potential was recorded for concentrations range from 5×10^{-4} to 5×10^{-2} M of standard solutions of drugs.

The obtained results are shown in Table 4 and the typical plot of electrode potential versus pH for electrode IB and IVB are shown in Figure 9.

Table4: Working pH ranges for TFP-MIP electrodes

Electrode No.	Membrane composition	PH range		
		5×10^{-2}	5×10^{-3}	5×10^{-4}
IB	TFP-MIP1(2-VP +DVB+DBS)	2.5 – 11.5	1.5 – 12.0	1.5– 11.0
IIB	TFP-MIP1(2-VP +DVB+NB)	3.5 – 10.5	3.0 – 10.5	3.0 – 10.0
IIIB	TFP-MIP2(2-HEMA+DVB+DBS)	1.5 – 10.5	2.5 – 9.5	3.5 – 11.5
IVB	TFP-MIP2(2-HEMA+DVB+NB)	3.0 – 12.0	3.5 – 11.5	3.0 – 11.0

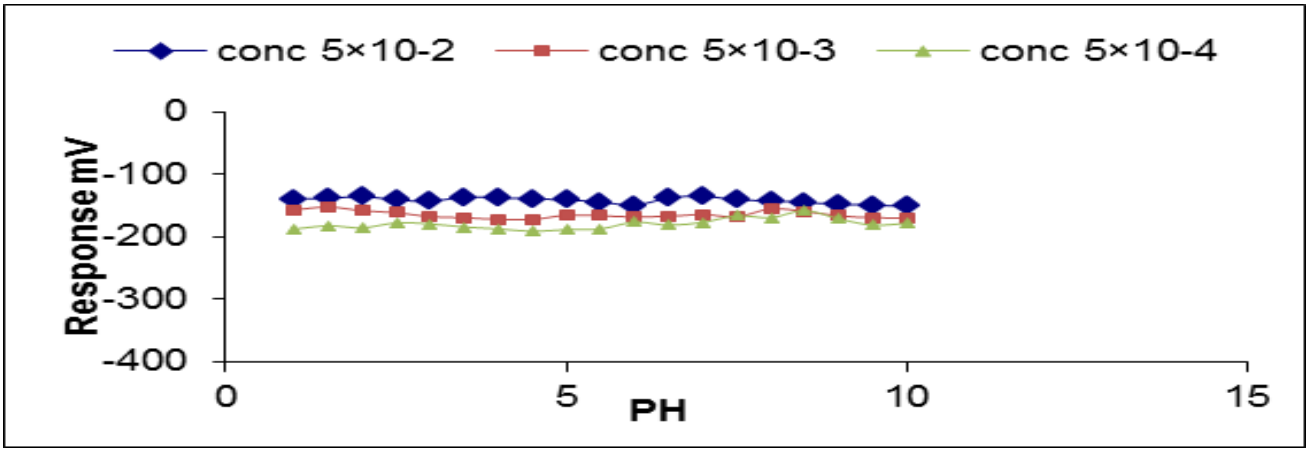


Figure.9: Typical plot of electrode response versus PH of electrode (IB) TFP-MIP1 (2-VP +DVB+DBS) at different concentration (5×10^{-2} , 5×10^{-3} , 5×10^{-4})

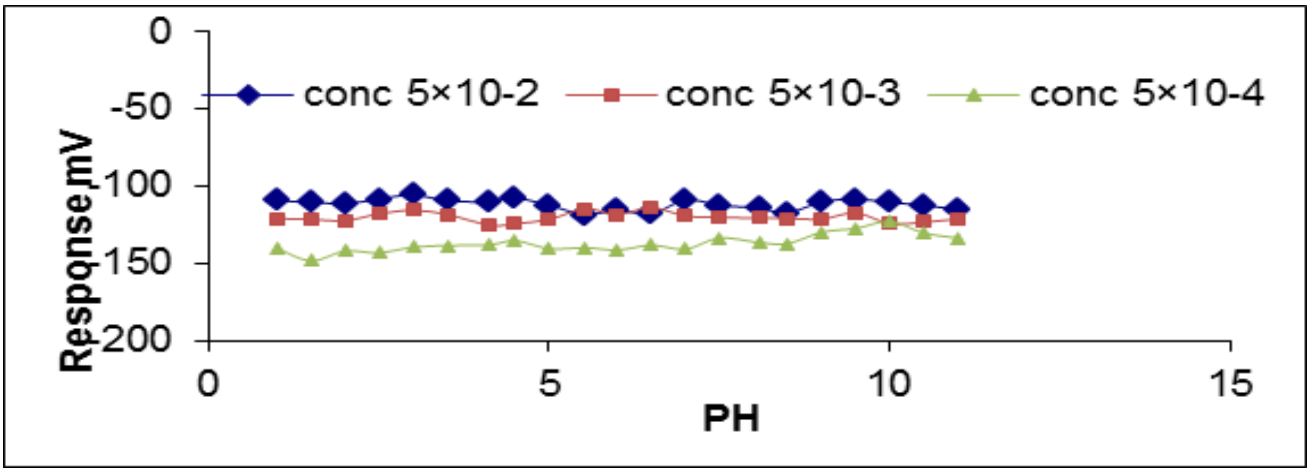


Figure.10: Typical plot of electrode response versus PH of electrode (IIB) TFP-MIP1 (2-VP +DVB+NB) at different concentration (5×10^{-2} , 5×10^{-3} , 5×10^{-4})

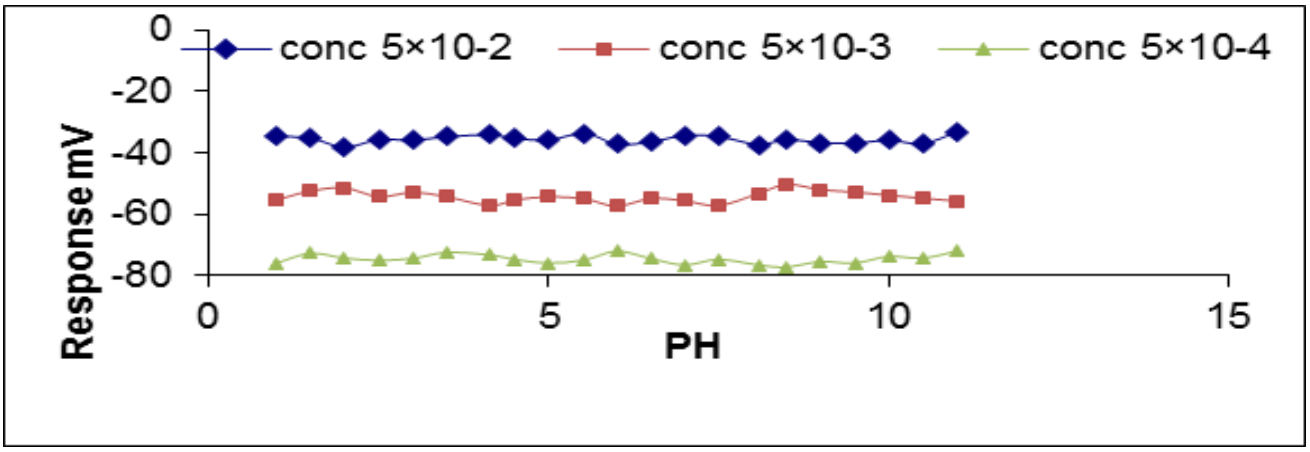


Figure11: Typical plot of electrode response versus PH of electrode (IIIB) TFP-MIP2 (2-HEMA+DVB+DBS) at different concentration (5×10^{-2}, 5×10^{-3}, 5×10^{-4})

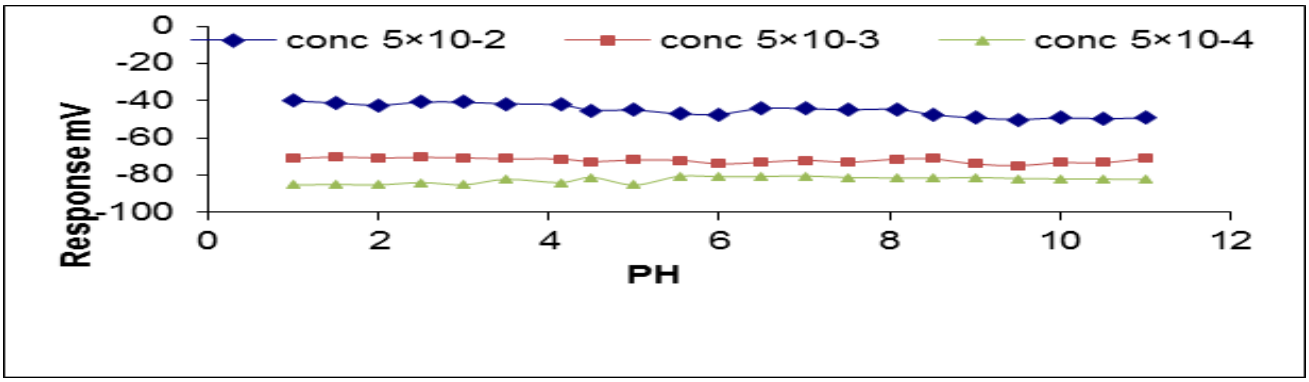


Figure12: Typical plot of electrode response versus PH of electrode (IVB) TFP-MIP2 (2-HEMA+DVB+NB) at different concentration (5×10^{-2}, 5×10^{-3}, 5×10^{-4})

Response Time and Life Time

The response time for all TFP.MIP electrodes was obtained from the dynamic potential response at concentration range between 1×10^{-6}– 1×10^{-1}M by measuring the time required to reach 95 % equilibrium potential. The results indicate that the response time of the electrodes were approximately 43.5 seconds for the solution of Trifluoperazine at high concentration 10^{-1}M and about 60.9seconds at low concentration10^{-6} M. The electrode lifetime was obtained by measuring the slope periodically from calibration curves for TFP-MIP during 40-50 days as shown in Table 5.

Table 5: Response time of Trifluoperazine electrodes

Membrane composition	Concentration (M)	Potential (mV) at t/100	Time (s) at 95%	Time (s) at 100%
TFP-MIP1(2-VP (+DVB+DBS)(IB)	10^{-1}	-141.5	29.7	30.2
	5×10^{-2}	-152.7	44.6	45.6
	5×10^{-3}	-168.2	51.2	52.5
	5×10^{-4}	-188.7	56.5	58.6
	5×10^{-5}	-210.4	56.9	59.2
	5×10^{-6}	-239.2	58.1	60.9
TFP-MIP1(2-VP (+DVB+NB)(IIB)	10^{-1}	-91.8	21.3	22.5
	5×10^{-2}	-101.5	30.2	31.8
	5×10^{-3}	-125.3	33	35.2
	5×10^{-4}	-141.4	37.4	40.1
	5×10^{-5}	-160.7	43.2	46.3
	5×10^{-6}	-186.2	45.5	49.7
TFP-MIP2(2-(HEMA+DVB+DBS)IIIB)	10^{-1}	-24.2	42.7	43.5
	5×10^{-2}	-33.5	46.1	47.6
	5×10^{-3}	-58.2	49.3	51.2
	5×10^{-4}	-75.6	52.4	54.7
	5×10^{-5}	-102.5	56.2	59.3
	5×10^{-6}	-120.3	56.8	60.2
TFP-MIP2(2-HEMA+DVB+NB)(IVB)	10^{-1}	-35.2	38.4	39.5
	5×10^{-2}	-44.6	39.8	41.7
	5×10^{-3}	-70.8	44.3	46.8
	5×10^{-4}	-95.4	47	50.6
	5×10^{-5}	-115.4	49.4	53.4
	5×10^{-6}	-135.7	55.2	59.6

Selectivity Coefficient

Potentiometric selectivity coefficients have been carried out by means of Separation Solution Method [13]. With using Trifluoperazine concentrations ranging (1×10^{-1}–5×10^{-6}) M plus diverse interfering substances (methyl paraben, propyl baraben, trisodium citrate, the potentiometric selectivity coefficients have been computed by equation below:

Log K pot A, B = (EB-EA) ZAF/2.303RT + (1-ZA/ZB) log AA…1

Where the interfering ions potential and KA, B values are indicated in plus the selectivity headed for the studied species are seen in Fig. (13) Till (16):

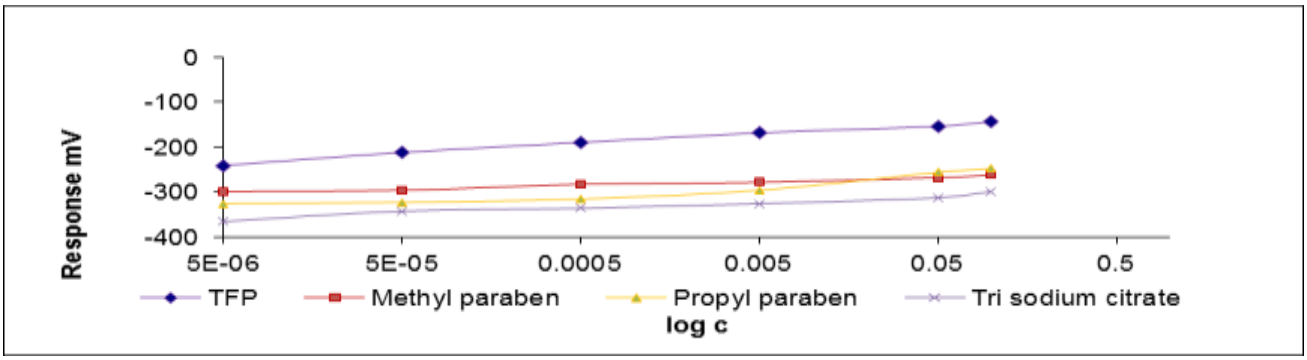


Figure13: Variation selectivity coefficient Log Kpot A, B With concentration at (a_A=a_B) using electrode TFP-MIP1 (2-VP +DVB+DBS) (IB) (Methyl paraben, propyl baraben , Tri sodiucitrate)

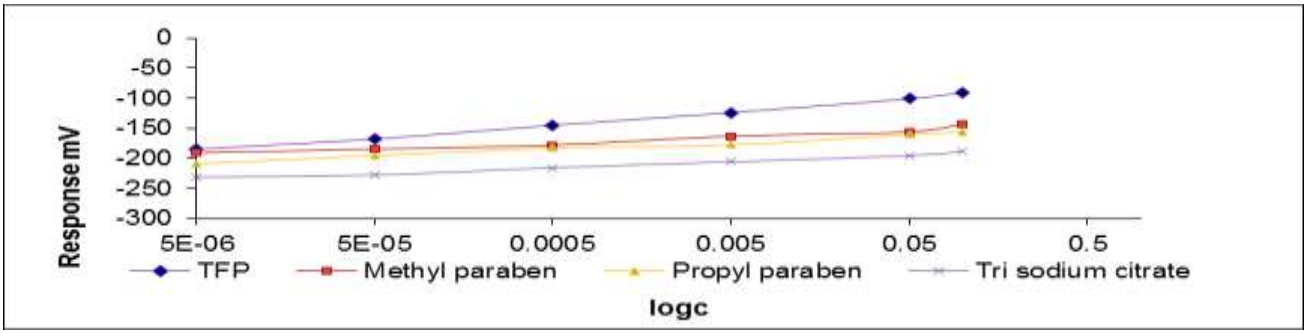


Figure14: Variation selectivity coefficient Log Kpot A,B With concentration at (a_A=a_B) using electrode TFP-MIP1(2-VP +DVB+NB)(IIB)(Methyl paraben , propyl baraben, Tri sodiucitrate)

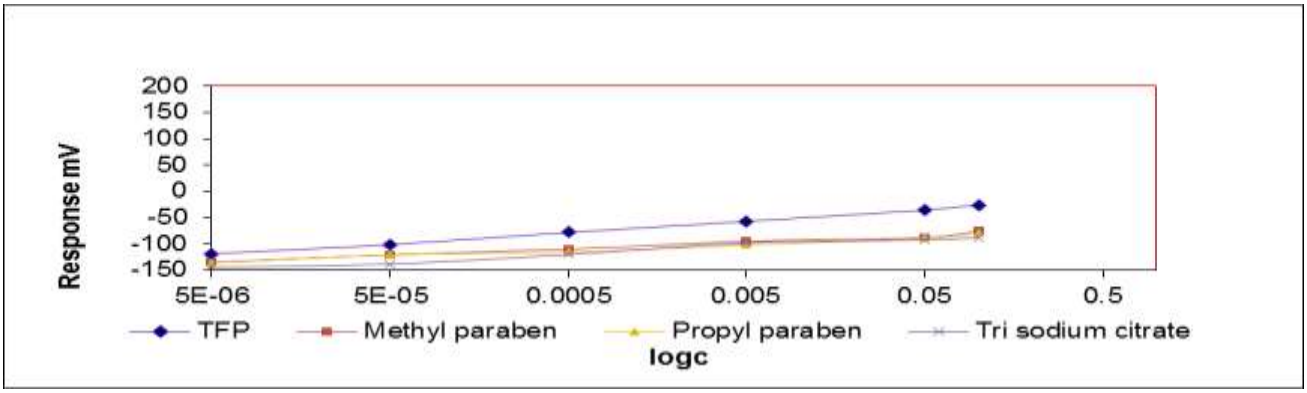


Figure15: Variation selectivity coefficient Log Kpot A,B With concentration at (a_A=a_B) using electrode TFP-MIP2(2-HEMA+DVB+DBS)(IIB)(Methyl paraben , propyl baraben , Tri sodium citrate)

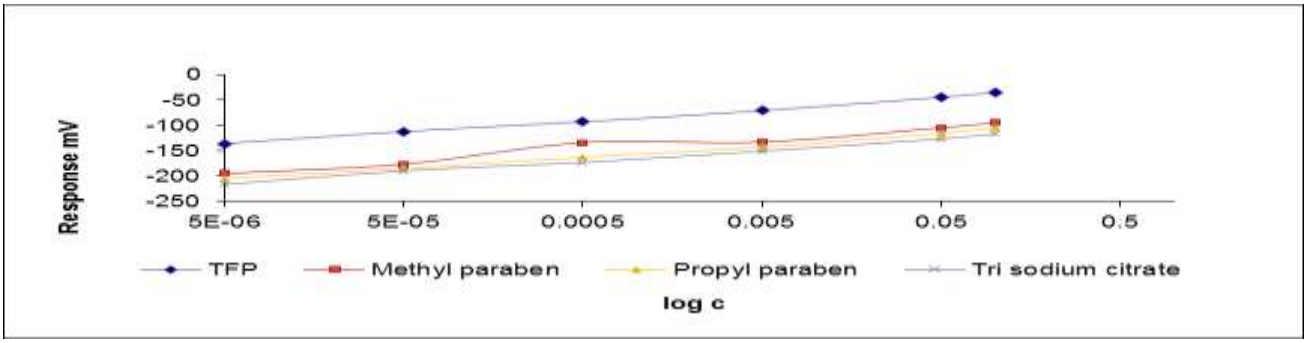


Figure16: Variation selectivity coefficient Log Kpot A,B With concentration at (a_A=a_B) using electrode TFP-MIP2(2-HEMA+DVB+NB) (IVB)(Methyl paraben , propyl baraben , Tri sodium citrate)

Quantitative Analysis

The accuracy of electrodes IB and IVB were measured by determining Trifluoperazine in synthetic solutions of 5×10^{-3} and 5×10^{-4} M using standard addition method. Excellent results of % recovery were obtained in the range 100.36 to 101.08. A typical plot for membrane IB and IVB at concentration of synthetic solution (5×10^{-3}, 5×10^{-4}) M is shown in Fig. (17 till 20) and the standard solution added was 0.1 M.

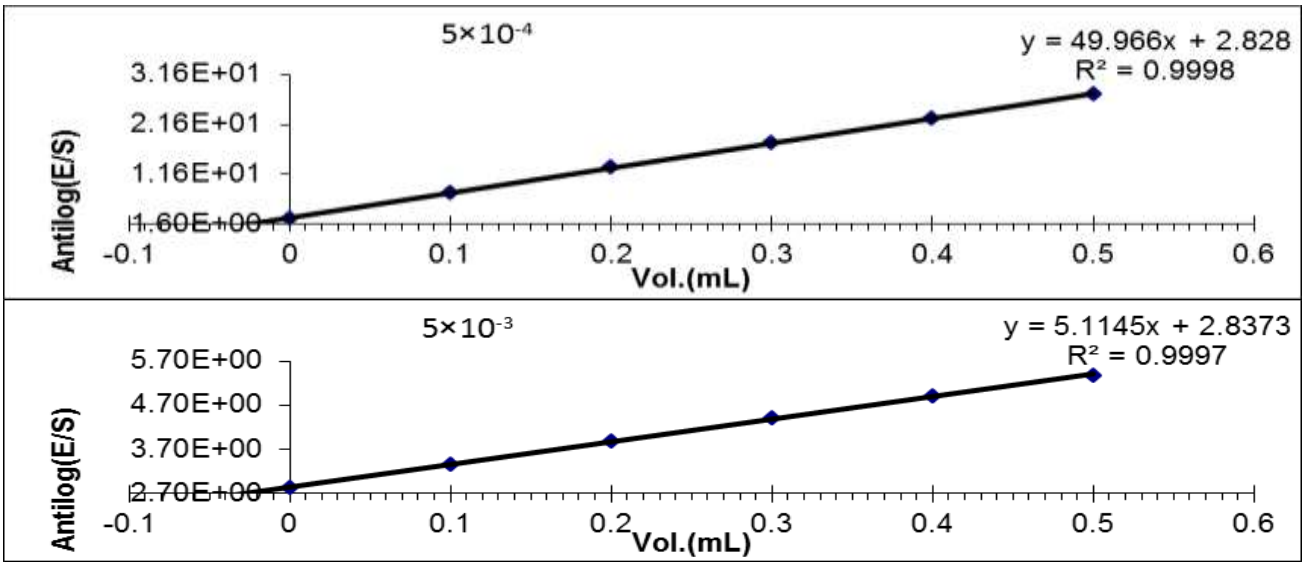


Fig.17. Variation of antilog (E/S) of synthetic solution of 5×10^{-3}, 5×10^{-4}M versus of standard TFP added using electrode (IB)

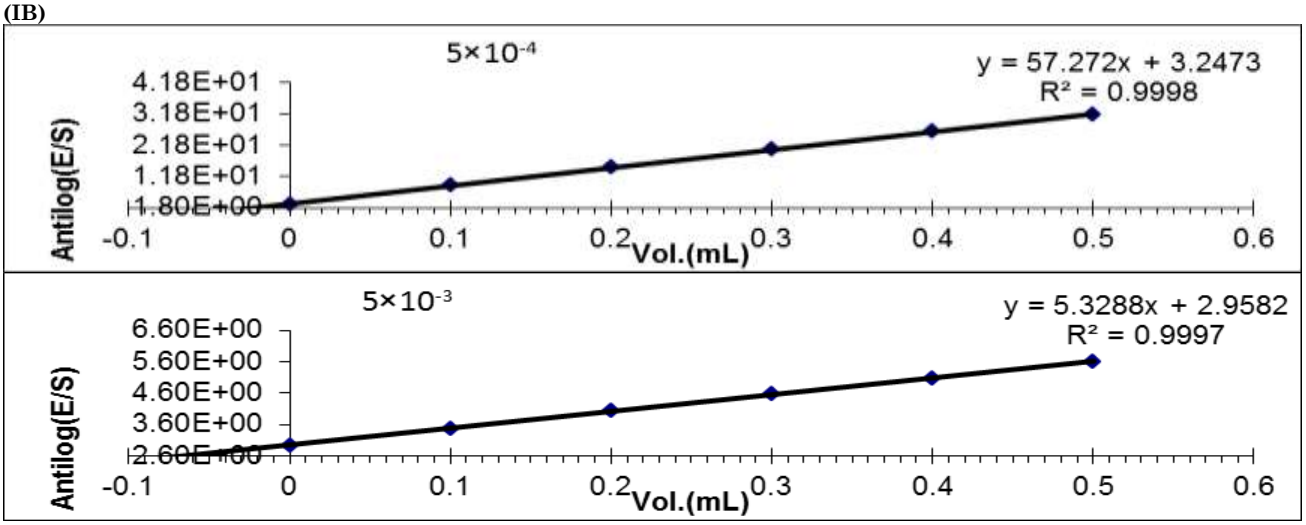


Fig.18. Variation of antilog (E/S) of synthetic solution of 5×10^{-3}, 5×10^{-4} M versus of standard TFP added using electrode (IIB)

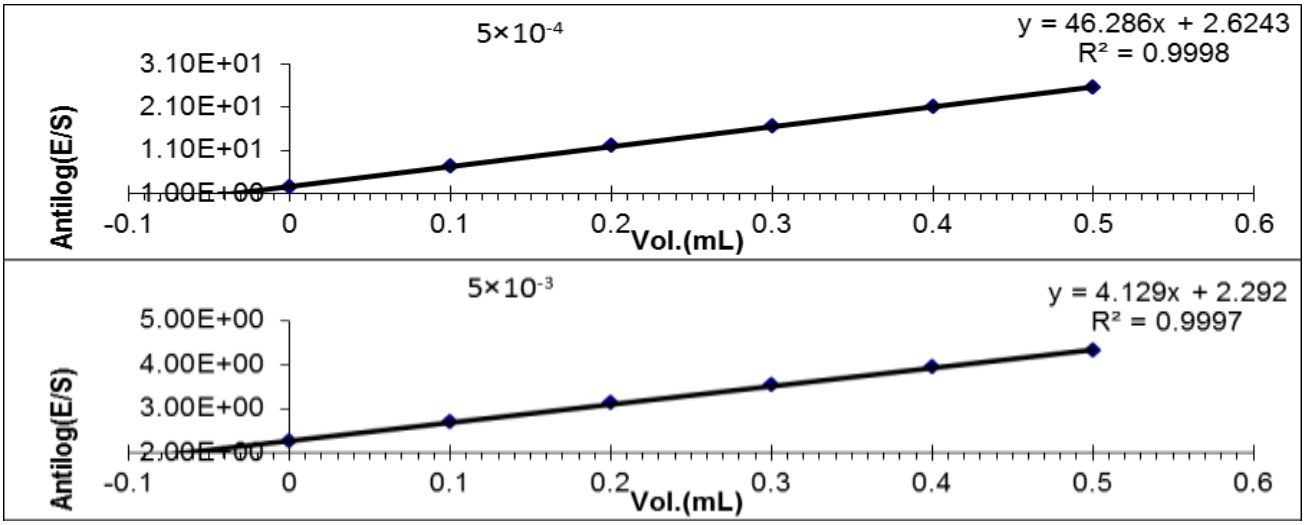


Fig.19. Variation of antilog (E/S) of synthetic solution of 5×10^{-3}, 5×10^{-4} M versus of standard TFP added using electrode (IIIB)

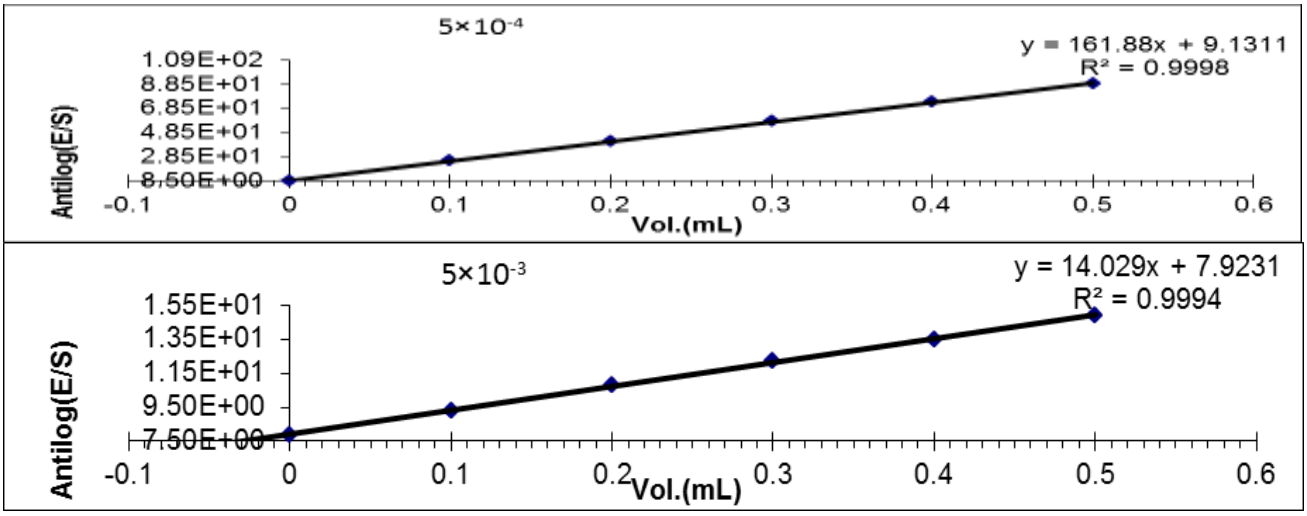


Fig.20. Variation of antilog (E/S) of synthetic solution of 5× 10^{-3}, 5×10^{-4} M versus of standard TFP added using electrode (IVB)

In order to be the proposed method of practical application has been taking two methods direct and standard additions method (SAM) was applied for types of commercial pharmaceutical tablets (Salabid 5 mg, Trifluoperazine 1mg) obtained membrane IB,IIB.IIIB and IVB. The values of the % recovery Table 6 were in a good agreement with the value given in British Pharmacopoeia [14]. There is no interference of all species on electrode response; therefore, the values of recovery obtained by standard additions method were in good agreement with the results of the direct method. There is no interference of all species on electrode response, therefore, the values of recovery obtained by standard additions method [15].Were in good agreement with the results of direct method.

Table 6: Results of recovery and standard deviation of commercial drugs obtained by using membrane IB, IVB

No. of electrode	Pharmaceutical Drug	Potentiometric methods	Concentration Prepared/ M	Concentration Found/ M	%Rec.	%RE	%RSD
IB	Samara-Salabid 5 mg	Direct method	5.0x10^{-3}	5.0212 x10^{-3}	100.42	0.42	1.20
		SAM		5.0134 x10^{-3}	100.26	0.26	1.13
		Direct method	5.0x10^{-4}	4.9114×10^{-4}	98.22	-1.77	1.42
		SAM		4.9102×10^{-4}	98.20	-1.79	1.38
IVB	Samara-Salabid 5 mg	Direct method	5.0x10^{-3}	5.0853×10^{-3}	101.70	1.70	1.23
		SAM		4.9747×10^{-3}	99.49	-0.50	1.31
		Direct method	5.0x10^{-4}	5.0325×10^{-4}	100.65	0.65	1.75
		SAM		5.0452×10^{-4}	100.90	0.90	1.41
IB	Ajanta Pharma-Trifloberazine 5mg	Direct method	5.0x10^{-3}	5.0518×10^{-3}	101.03	1.03	2.12
		SAM		4.9525×10^{-3}	99.05	-0.95	1.18
		Direct method	5.0x10^{-4}	4.9912 x10^{-4}	99.82	-0.17	2.21
		SAM		5.0221 x10^{-4}	100.44	0.44	1.51
IVB	Ajanta Pharma-Trifluoberazine 5mg	Direct method	5.0x10^{-3}	5.0945×10^{-3}	101.89	1.89	1.81
		SAM		5.0822×10^{-3}	101.64	1.64	2.32
		Direct method	5.0x10^{-4}	4.9124 x10^{-4}	98.24	-1.75	1.75
		SAM		5.0965 x10^{-4}	101.93	1.93	1.05

Conclusion

Trifluoperazine The construct ion of molecularly imprinted electrodes sensors (MIP) using Trifloberazine as a template and Divinylbanzene (DVB) as cross-linkers and (2-vinyl pyridine (2V-P), and 2-hydroxy ethyl meth acrylate (2-HEMA) as monomers in different plasticizers. results of MIP that Showing high sensitivity, reasonable selectivity, fast response and stable long-term stability and the possibility of widely applied pH were obtained by using electrode based on DBS and NB plasticizers. Good results of recoveries were obtained for the determination of Trifluoperazine in the commercial tablets in comparison with the British Pharmacopoeia.

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