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SYNTHESIS NEW MOLECULARLY IMPRINTED POLYMERS FOR THE SELECTIVE ELECTRODES OF ISOPROPAMIDE FROM PHARMACEUTICAL SAMPLES

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Keywords:

Molecularly imprinted electrodes, Isopropamide, Potentiometric method, (2-HEMA), (2-VP) monomers

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ABSTRACT: Liquid electrodes of polymers imprinted with Isopropamide (ISP) were synthesized based on precipitation polymerization mechanism. The molecularly imprinted polymer (MIP) and non-imprinted polymers (NIP) were synthesized using (ISP) as a template. In the polymerization process, 2-Hydroxyethyl meth acrylate (2-HEMA) and 2-Vinyl pyridine (2-VP) were used as monomers. Di-vinylbanzene (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 using dibutyl sebacate (DBS) and nitrobenzene (NB) as plasticizers in PVC matrix. Slopes and detection limit of the liquid electrodes are ranged at (52.23-58.94) mV/decade and (1.2×10^{-6} - 2.0×10^{-5}) M, respectively. Response time was 60 sec. Liquid electrodes were filled with 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 over several species. The new synthesis electrodes were successfully used for the analyte estimated in preparation pharmaceutical sample without any time-consuming pre-treatment steps.

INTRODUCTION: Isopropamide (R5) is a long-acting anticholinergic drug [1]. It is used in the treatment of peptic ulcers and other gastrointestinal disorders involving hyperacidity (gastrointestinal acidosis) and hypermotility [2]. Chemically, it contains a quaternary ammonium group [3]. It is most often provided as an iodide salt but is also available as a bromide or chloride salt. It was discovered at Janssen Pharmaceutica in 1954. Molecularly imprinted polymers (MIPs), generally behave as synthetic antibody snob, have been appearing to be very promising candidates as highly selective adsorbents, because of the advantages inherent such as reusability, physiochemical, molecular specificity, stability and applicability in harsh chemical media [4].

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MIPs are mainly based on the polymerization of functional monomers in the presence of a template molecule. The template is leached out leaving behind cavities which are integral in shape, size, and functionality to the template.

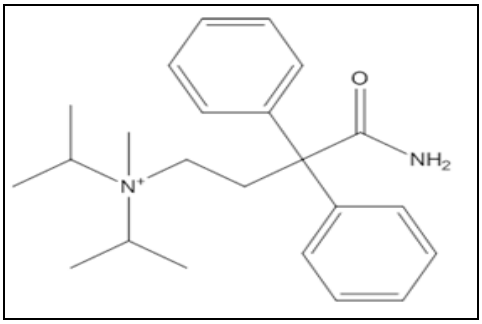

FIG. 1: STRUCTURE ISOPROPAMIDE DRUG (ISP)

In recent years, MIP technology has developed to a valuable integral concept for biological activity with increased applicability in analytical chemistry, which show different and rapid methods for synthesis a polymer matrix with molecule-specific activity properties with applications ranging from purification of racemic mixtures 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 Isopropamide as a template in PVC matrix membrane and electrodes specification was studied.

EXPERIMENTAL:

Chemicals: Isopropamide was obtained from the State Company of Drug Industries and Medical Appliances (IRAQ-SDI Samara, Ajanta Pharma, India). The commercial Isopropamide tablets obtained from local stores is Salabid 5 mg and Isopropamide 5 mg. Nitrobenzene (NB) (99%), and dibutyl sebacate (DBS) (99%), as well as metal salts, were purchased from Sigma-Aldrich and were used as they were received. 2-Hydroxyethyl methacrylate (2-HEMA) (99%), 2- Vinyl pyridine (2-VP) (99%). Divinylbanzene (DVB) (99%), band benzoyl peroxide (BPO) (78%) was purchased from Sigma-Aldrich. The chemicals used in the search were possessed high purity does not need to purify.

Apparatus: Potentiometric measurements were carried out with a digital voltmeter (HANA pH 211 instrument Microprocessor pH meter). pH measurements were made 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) SHIMADZU (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 and Sohn GmbH, Germany.

The performance of the electrode was investigated by measuring the potential of Isopropamide solutions at room temperature with a concentrations range from 10^{-1} to 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 the preparation of MIP. The template (ISP) of 0.4mmol was dissolved in a thick-walled glass tube (50 ml capacity) filled with 10 ml chloroform. Two monomers were used for the preparation of MIP, 2 mmole of 2-vinyl pyridine (2V-P) with 9.99 mmole divinylbenzene (DVB) as a cross-linker, the second MIP based on 4.6 mmol of 2-hydroxyethyl methacrylate (2-HEMA) as a monomer with 9.99 mmole divinyl benzene as cross-linker. The initiator of 0.2 mmole BPO was used. The solution was mixed in an ultrasonic water bath for 45 min [8], during this time the nitrogen gas has purged the mixture [9]. After 45 min seals the tube and put the tube in 65 °C water bath to permit starting the reaction which continued for 2 days. The templates were removed by repeated washing 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) h. 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 was completely dried at ambient temperature, it was used as active material in the selective sensor membrane [10].

The non-printed polymer NIP was made in the same way but without the template drug. To prepare specific PVC membrane, high molecular weight PVC (0.17 g) mixed with the MIP (0.036 g) and the plasticizer (0.4 g) until the solution becomes homogenized, and then add THF (5-6 ml) and stirred. The solution was transferred to glass vessel based on glass board with 5 cm dia. circular section to let this mixture evaporate for 24 h. A glass tube contains a silver wire painted with silver chloride and filled with 0.1 M standard solution of Isopropamide was connected to one end of the tygon tube tightly while the second end of the tube was attached to 10 mm dia. [11] circular disk of the PVC membrane by using a concentrated PVC/THF solution as a glue in the 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 Isopropamide before and after washing is showed by electron microscope in **Fig. 2**. A porous on the surface **Fig. 2A** about 20 μm may indicate the binding sides to the polymer. **Fig. 2B** shows clear holes about 50μm in sizes have been obtained and which were removed by Soxhlet extraction.

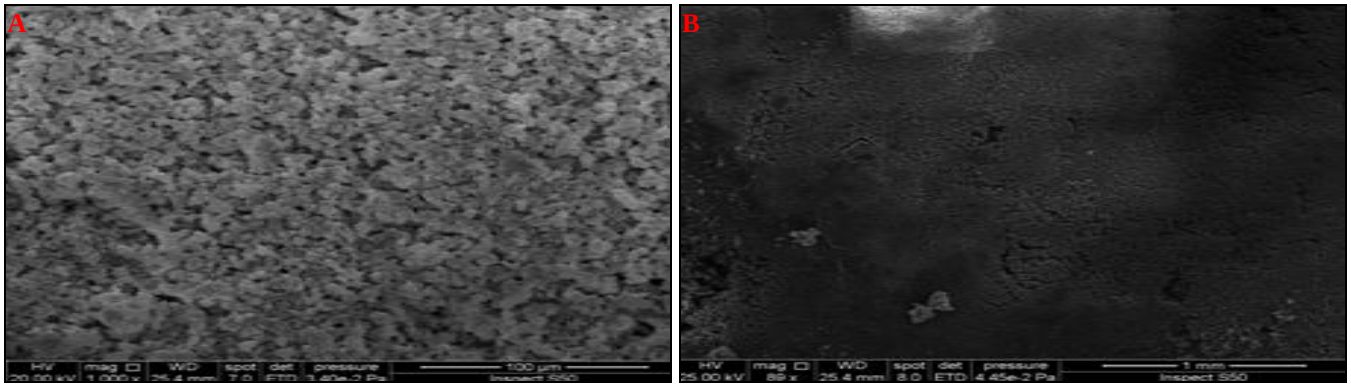

FIG. 2: SEM PHOTOGRAPH OF THE SURFACE OF MIP, A) AFTER WASHING B) BEFORE WASHING

Potential Measurements: Measurements were carried out in a 50 ml double walled glass cell, magnetic stirring was used to obtaining 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 5×10^{-1} to 5×10^{-6} M by serial dilution. The slope, detection limit, and response time operative life were calculated from the calibration curve.

Preparation of Pharmaceutical Samples: Three types of tablets were used to determine the concentration of Isopropamide, 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) (Isopropamide) capsules were grinded (0.0275 g) and dissolved in 1M (HCl) and completed in volumetric flask to (100 ml).

RESULTS AND DISCUSSION:

Characterization: The FT-IR spectra of the ISP, ISP-MIP, two imprinted polymers based on (2-Vinyl pyrdine) as a basic functional monomer (before and after the removal of the drug) and their nonimprinted polymers are shown in **Fig. 3-5** for (ISP) drug. **Table 1** summarized the main peaks that appeared in these figures. In spectrum (3) for drug we can see two sharp bands for asymmetrical and symmetrical N-H stretching and a band of 1664 cm^{-1} for carbonyl stretching of amide. While in the spectrum (4) before show band at 1728 cm^{-1} for ester carbonyl stretching and band and 1629 cm^{-1} for olefine C=C stretching group which does not exist in the drug spectrum.

The spectrum also shows strong bands at 2958 cm^{-1} and 2856 cm^{-1} for asymmetrical and symmetrical aliphatic C-H stretching.

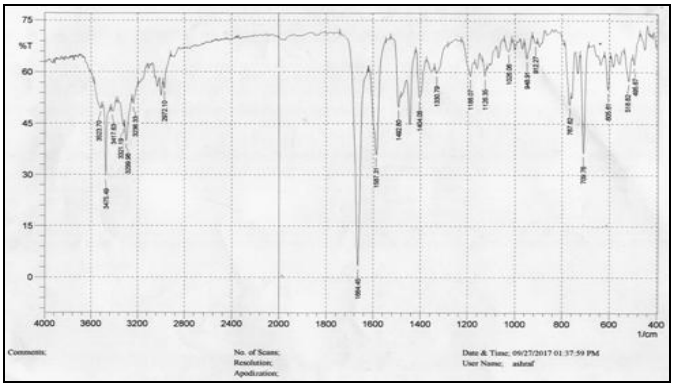

FIG. 3: FTIR OF (ISP) DRUG

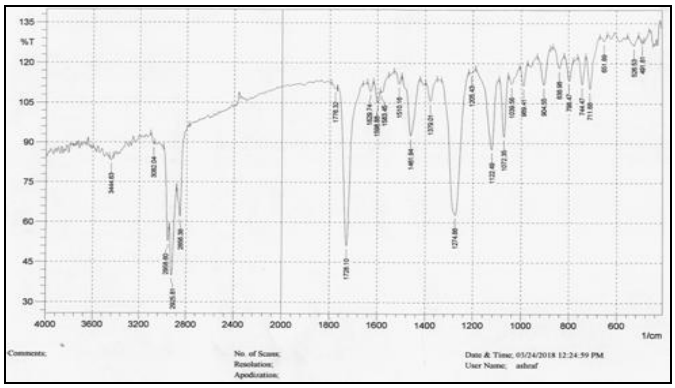

FIG. 4: FTIR OF ISP-MIP (2-VP) BEFORE THE REMOVAL OF (ISP)

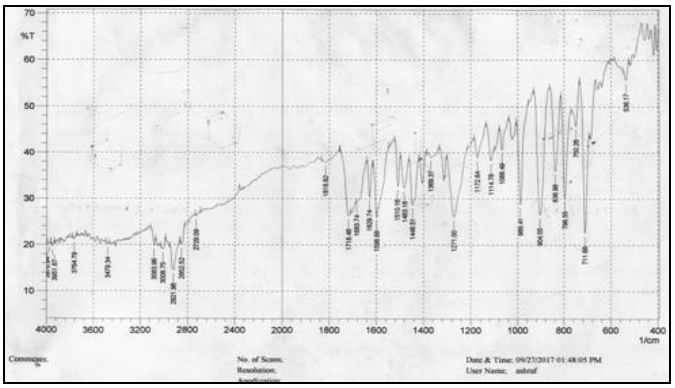

FIG. 5: FTIR OF ISP-MIP (2-VP) AFTER THE REMOVAL OF (ISP)

TABLE 1: THE MOST IDENTIFIED PEAKS OF FTIR SPECTRA FOR ISP-IMPRINTED POLYMER USING (2-VP) AS A FUNCTIONAL MONOMER

S. no.	Functional Group	Drug (ISP)	ISP-MIP (2-VP) before Template removal	ISP-MIP (2-VP) after Template removal
1	N-H str. (cm^{-1})	Asym 3475, sym 3299	3444	-
2	C=O str. amide.(cm-1)	1664	1629	-
3	C=C aromatic.(cm^{-1})	1587	1598, 1583	1598
4	C-H str. alphatic. (cm^{-1})	2972	2958, 2856	2921, 2852
5	Out-of plane bending	767,709	744,711	750, 711
6	C-H aromatic. (cm^{-1})	3050	3082	3083
7	C=O str. ester (cm^{-1})	-	1728	1718
8	C=C olefiine	-	1629	1629

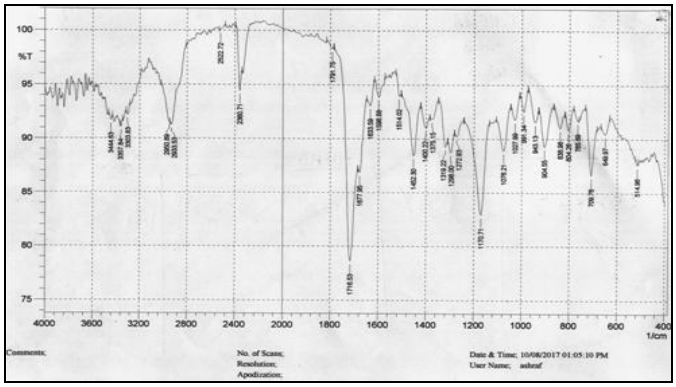

FIG. 6: FTIR OF ISP-MIP (2-HEMA) BEFORE THE REMOVAL OF (ISP)

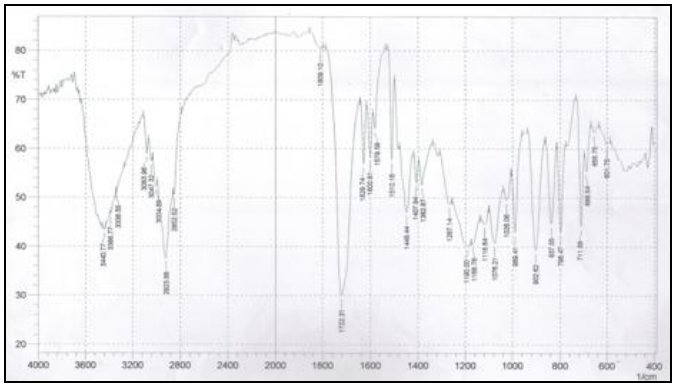

FIG. 7: FTIR OF ISP-MIP (2-HEMA) AFTER THE REMOVAL OF (ISP)

TABLE 2: THE MOST IDENTIFIED PEAKS OF FT-IR SPECTRA FOR ISP-MIP USING (2-HEMA) AS A FUNCTIONAL MONOMER

S. no.	Functional Group	Drug (ISP)	ISP-MIP (2-HEM) before Template removal	ISP-MIP (2-HEM) after Template removal
1	N-H str. (cm^{-1})	Asym 3475, sym 3299	3444, 3303	-
2	C=O str. amide. (cm-1)	1664	1677	-
3	C=C aromatic.(cm^{-1})	1587	1598	1600.8
4	C-H str. alphatic. (cm^{-1})	2972	2950,2933	2923,2852
5	O-H str. (cm^{-1})	-----	3357(b)	3440(b)
6	C=O str. ester (cm^{-1})	-----	1716	1722
7	C=C olefiine (cm^{-1})	-----	1633	1629

Spectrum (5) after showing the disappearance and N-H stretching bands and the carbonyl of amide stretching band which give a good indication for the elimination of drug molecule from the polymer. The spectra of FTIR for the ISP, ISP-MIP based on (2-HEMA) as an acidic functional monomer (before and after the removal of the template) and their nonimprinted polymers are shown in **Fig. 6-7** for (ISP) drug. **Table 2** summarized the main peaks that appeared in these figures.

In spectrum (3) for the drug we can see sharp bands at 3475 cm^{-1} and 3299 cm^{-1} for N-H asymmetrical and symmetrical stretching and very strong a sharp band at 1664 cm^{-1} for carbonyl stretching of the amide group. The spectrum (6) before show broadband for hydroxyl group stretching for the monomer 2-HEMA as well as a band at 1716 cm^{-1} which attributed to the carbonyl stretching of aster group. And as we see the value is low due to conjugation, the spectrum also shows at 1633 cm^{-1} for C=C olefine stretching which higher than aromatic one. The band at 1677 cm^{-1} for aromatic carbonyl stretching and 1598 cm^{-1} for C=C aromatic stretching bands at 3444 cm^{-1} and 3303 cm^{-1} for asymmetrical and symmetrical N-H stretching. The spectrum (7) after showing the dis-appearance of N-H stretching bands and the broad appearance band at 3440 cm-1 for O-H stretching and strong bands for C-H aliphatic stretching, also we see the disappearance of carbonyl stretching band of amide group and the appearance of strong band for ester carbonyl stretching.

Liquid Membranes Electrode: MIP based liquid electrodes, their concentrations range and slopes response to Nernstian equation have been investigated. The membranes of MIP made of the monomers 2-HEMA and 2-VP with a PVC matrix using two plasticizers DBS and NB. The internal solution was used 0.1M standard aqueous solution of the drug for all liquid electrodes. Experimental results of the synthesis of molecularly imprinted (MIP) and non-imprinted polymers (NIP) based on two monomers 2-HEMA and 2-VP indicate that both monomers can be used for the preparation of effective MIP for Isopropamide. The plasticizer is an essential part of the sensing membrane, which has important role as a solvent for the different components and determines the mobility of the analyte in membrane. Both of the plasticizers that are used, DBS and NB, are suitable for the fabrication of MIP-based Isopropamide electrodes.

Table 2 shows the parameters of the fabricated and tested electrodes, Four membranes of the different compositions were prepared using two different plasticizers with different viscosities, dibutyl sebacate (DBS) (ν=11.0042cSt) and nitro benzene (NB) (ν = 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 19.62-57.36 mV/decade and linear dynamic ranges between 1.2×10^{-6} - 2.0×10^{-5} M. In generally the preparation electrodes have a short response time (about 60 sec) mostly at high concentrations.

The values listed in **Table 3** also indicate the electrodes IT, and IVT gives good results; therefore, the liquid electrode was used to determine both drugs in pharmaceutical samples.

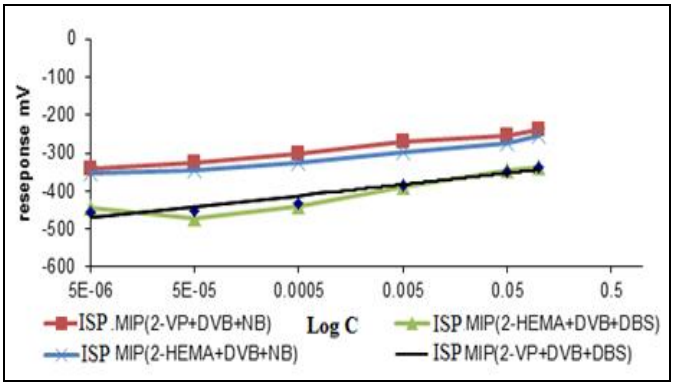

FIG. 8: CALIBRATION CURVES OF ISOPROPAMIDE-SELECTIVE ELECTRODES: IT, IIT, IIIT, IVT

TABLE 3: PARAMETER OF ISP-MIP ELECTRODES BASED ON DIFFERENT PLASTICIZERS

Electrode No.	Membrane Composition	Parameter				
		Slope (mV/dec.)	Detection limit (M)	Correlation coefficient	Linearity range (M)	Life time
IT	ISP -MIP1 (2-VP +DVB+DBS)	29.50	7×10^{-6}	0.944	6×10^{-6}-1×10^{-1}	40
IIT	ISP-MIP1 (2-VP +DVB+NB)	23.37	4×10^{-6}	0.986	1×10^{-5}-1×10^{-1}	50
IIIT	ISP-MIP2 (2-HEMA+DVB+DBS)	29.90	6×10^{-6}	0.838	5×10^{-5}-1×10^{-1}	45
IVT	ISP-MIP2 (2-HEMA+DVB+NB)	23.12	6×10^{-6}	0.964	5×10^{-5}-1×10^{-1}	40

Influence of pH: The effect of pH on the potential values of the four electrodes 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 NaOH to the aqueous solutions of the drugs and the obtained potentials at each value were recorded.

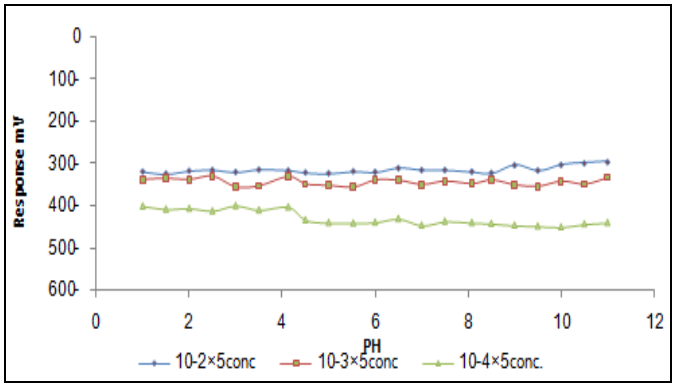

FIG. 9: TYPICAL PLOT OF ELECTRODE RESPONSE *vs.* pH OF ELECTRODE ISP-MIP1 (2-VP+DVB+DBS) AT DIFFERENT CONCENTRATION (5×10^{-2}, 5×10^{-3}, 5×10^{-4})

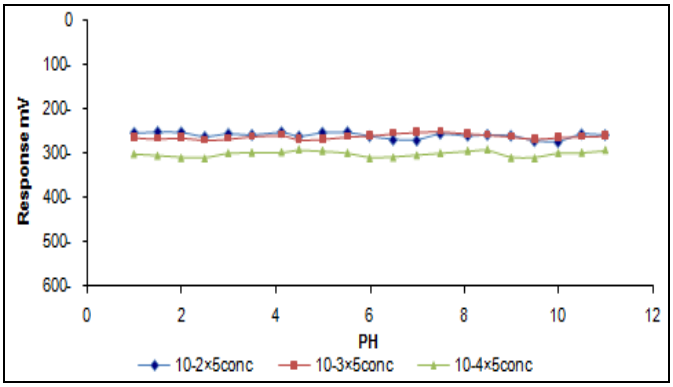

FIG. 10: TYPICAL PLOT OF ELECTRODE RESPONSE *vs.* pH OF ELECTRODE ISP-MIP (2-VP+DVB+NB) AT DIFFERENT CONCENTRATION (5×10^{-2}, 5×10^{-3}, 5×10^{-4})

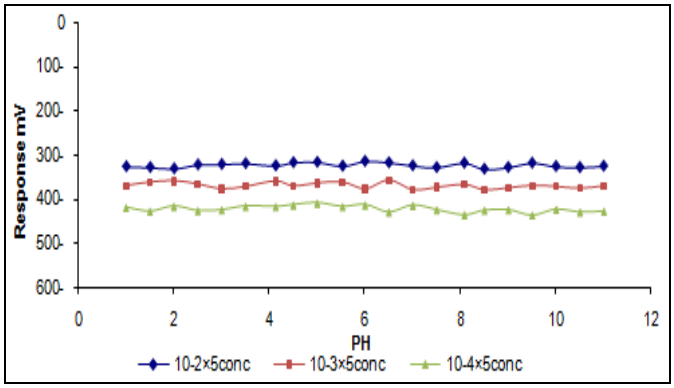

FIG. 11: TYPICAL PLOT OF ELECTRODE RESPONSE *vs.* pH OF ELECTRODE ISP-MIP (2-HEMA+DVB+DBS) AT DIFFERENT CONCENTRATION (5×10^{-2}, 5×10^{-3}, 5×10^{-4})

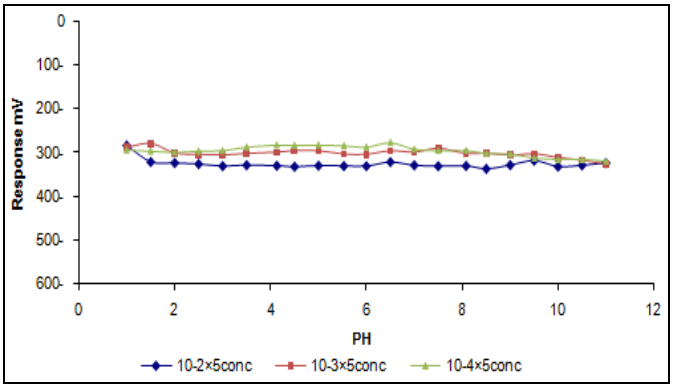

FIG. 12: TYPICAL PLOT OF ELECTRODE RESPONSE *vs.* pH OF ELECTRODE ISP-MIP (2-HEMA+DVB+NB) AT DIFFERENT CONCENTRATION (5×10^{-2}, 5×10^{-3}, 5×10^{-4})

TABLE 4: WORKING pH RANGES FOR ISP-MIP ELECTRODES

Electrode No.	Membrane Composition	pH range		
		5×10^{-2}	5×10^{-3}	5×10^{-4}
IT	ISP-MIP1 (2-VP +DVB+DBS)	1.5 – 8.5	2.0 – 9.0	2.0 – 7.5
IIT	ISP-MIP1 (2-VP +DVB+NB)	3.0 – 5.5	1.5 – 11.4	2.5 – 9.5
IIIT	ISP-MIP2 (2-HEMA+DVB+DBS)	4.0 – 6.5	4.0 – 6.5	4.5 – 9.0
IVT	ISP-MIP2 (2-HEMA+DVB+NB)	2.0 – 8.5	1.5 – 7.5	1.0 – 8.5

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 IT and IVT are shown in **Fig. 9-12**.

Response Time and Life Time: The response time for all ISP-MIP electrodes was obtained from the dynamic potential response at a 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 was approximately 48.7 sec for the solution of Isopropamide at high concentration 10^{-1} M and about 64.3 sec at low concentration 10^{-6} M. The electrode lifetime was obtained by measuring the slope periodically from calibration curves for ISP-MIP during 30-50 days as shown in **Table 5**.

TABLE5: RESPONSE TIME OF ISOPROPAMIDE ELECTRODE

Membrane composition	Concentration (M)	Potential (mV) at t/100	Time (s) At 95%	Time (s) At 100%
IT	10^{-1}	-332.3	46.4	48.7
	5×10^{-2}	-346.1	48.8	51.3
	5×10^{-3}	-382.5	58.4	61.2
	5×10^{-4}	-428.7	58.7	61.8
	5×10^{-5}	-447.2	59.1	62.5
	5×10^{-6}	-452.4	60.6	64.3
IIT	10^{-1}	-239.5	18.6	19.5
	5×10^{-2}	-254.6	28.8	30.2
	5×10^{-3}	-268.7	35.6	37.3
	5×10^{-4}	-301.5	38.5	40.6
	5×10^{-5}	-322.4	48.6	51.4
	5×10^{-6}	-340.5	50.3	53.5
IIIT	10^{-1}	-335.8	34	35.9
	5×10^{-2}	-342.2	48.7	50.8
	5×10^{-3}	-387.4	51.6	54.3
	5×10^{-4}	-441.5	54	57.2
	5×10^{-5}	-467.6	55.3	59.4
	5×10^{-6}	-444.8	56.2	60.5
IVT	10^{-1}	-255.3	39.8	41.5
	5×10^{-2}	-274.3	44.3	46.2
	5×10^{-3}	-296.3	47.2	49.5
	5×10^{-4}	-328.2	49.6	52.3
	5×10^{-5}	-349.1	54.4	57.5
	5×10^{-6}	-355.6	56.6	60.8

Selectivity Coefficient: Potentiometric selectivity coefficients have been carried out using separation solution method [13] with using Isopropamide concentrations ranging (1×10^{-1} - 5×10^{-6}) M plus diverse interfering substances (methylparaben, propyl paraben, trisodium citrate, the potentiometric selectivity coefficients have been computed by the equation below:

$$\log K^{pot}_{A,B} = (E_B - E_A)ZAF/2.303RT + (1-ZA/ZB) \log A_a \quad \text{….....3-1}$$

Where, the interfering ions potential and KA, B values are indicated in plus the selectivities headed for the studied species are seen in **Fig. 13-16**.

Quantitative Analysis: The accuracy of electrodes IT and IIIT were measured by determining Isopropamide in synthetic solutions of 5×10^{-3} and 5×10^{-4} M using the standard addition method. Excellent results of % recovery were obtained in the range 94.95 to 105.6.

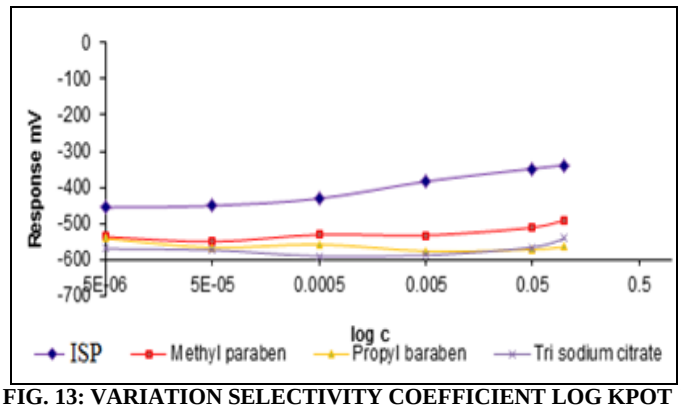

FIG. 13: VARIATION SELECTIVITY COEFFICIENT LOG KPOT A, B WITH CONCENTRATION AT (a_A=a_B) USING ELECTRODE ISP-MIP (2-VP+DVB+DBS) (METHYL PARABEN, PROPYL BARABEN, TRI-SODIUM CITRATE)

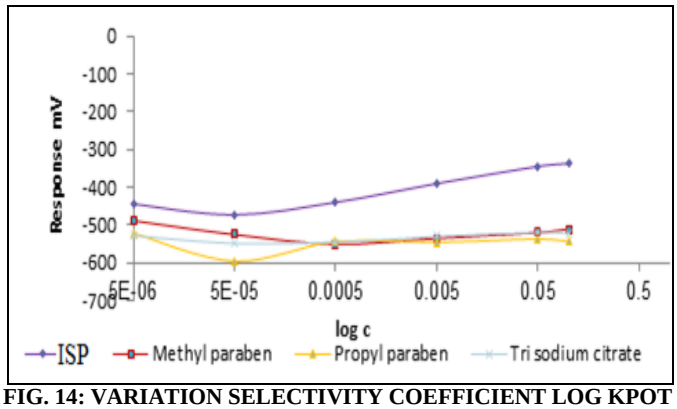

FIG. 14: VARIATION SELECTIVITY COEFFICIENT LOG KPOT A, B WITH CONCENTRATION AT (a_A=a_B) USING ELECTRODE ISP-MIP (2-VP+DVB+NB) (METHYL PARABEN, PROPYL BARABEN, TRI-SODIUM CITRATE)

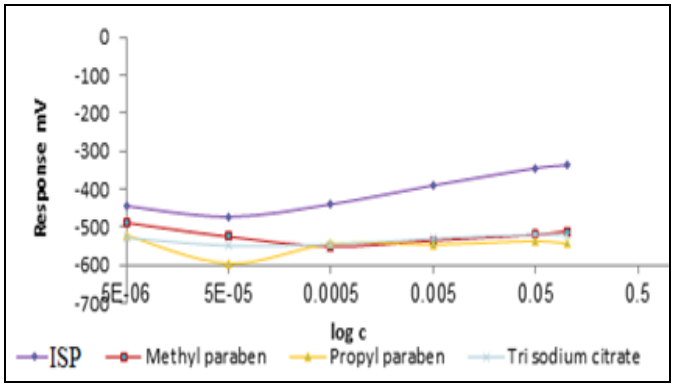

FIG. 15: VARIATION SELECTIVITY COEFFICIENT LOG KPOT A, B WITH CONCENTRATION AT (a_A=a_B) USING ELECTRODE ISP-MIP (2-HEMA+DVB+DBS) (METHYL PARABEN, PROPYL BARABEN, TRI-SODIUM CITRATE)

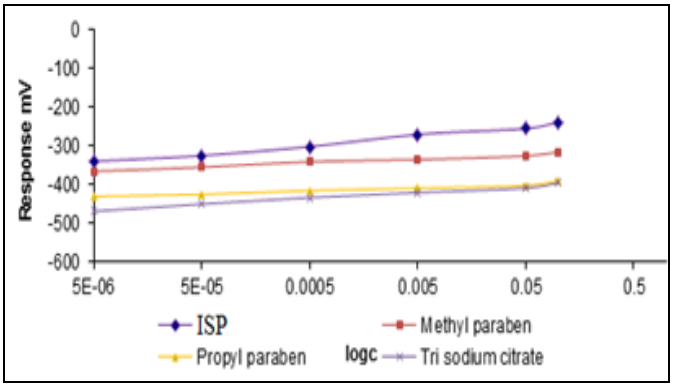

FIG. 16: VARIATION SELECTIVITY COEFFICIENT LOG KPOT A, B WITH CONCENTRATION AT (a_A=a_B) USING ELECTRODE ISP-MIP (2-HEMA+DVB+NB) (METHYL PARABEN, PROPYL BARABEN, TRI-SODIUM CITRATE)

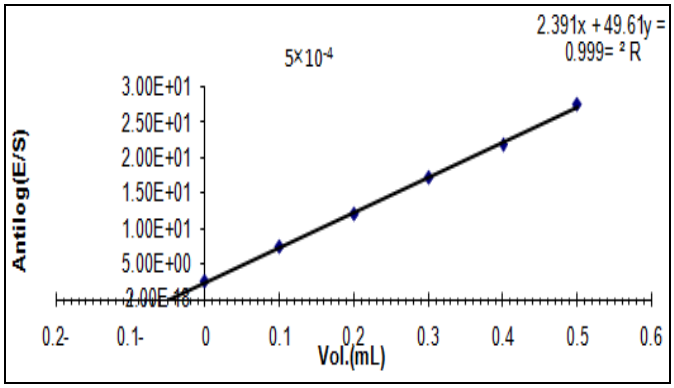

FIG. 17: VARIATION OF ANTILOG (E/S) OF SYNTHETIC SOLUTION OF 5×10^{-4} M vs. OF STANDARD ISP ADDED USING ELECTRODE (2-VP+DVB+DBS)

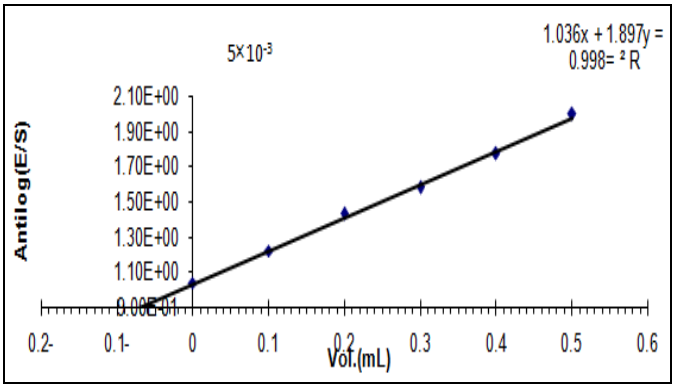

FIG. 18: VARIATION OF ANTILOG (E/S) OF SYNTHETIC SOLUTION OF 5×10^{-3} M *vs.* OF STANDARD ISP ADDED USING ELECTRODE (2-VP+DVB+DBS)

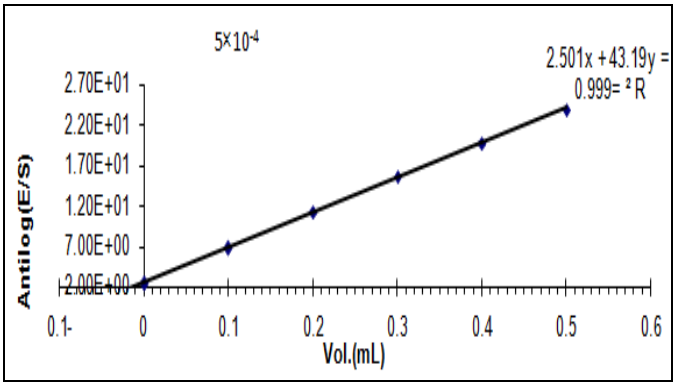

FIG. 19: VARIATION OF ANTILOG (E/S) OF SYNTHETIC SOLUTION OF 5×10^{-4} M *vs.* OF STANDARD ISP ADDED USING ELECTRODE (2-VP+DVB+NB)

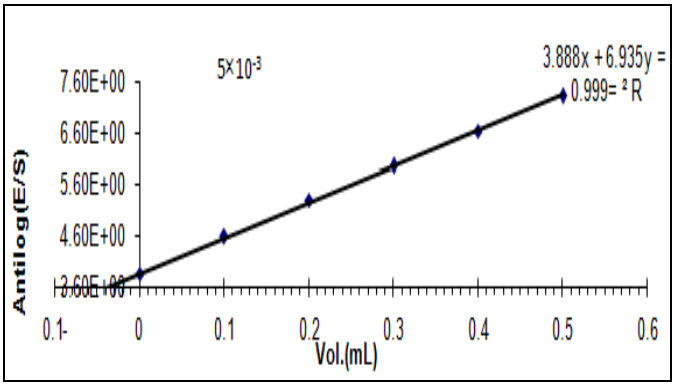

FIG. 20: VARIATION OF ANTILOG (E/S) OF SYNTHETIC SOLUTION OF 5× 10^{-3} M *vs.* OF STANDARD ISP ADDED USING ELECTRODE (2-VP+DVB+NB)

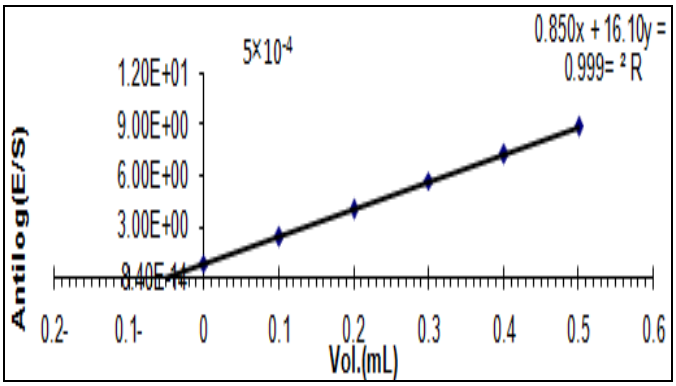

FIG. 21: VARIATION OF ANTILOG (E/S) OF SYNTHETIC SOLUTION OF 5×10^{-4} M *vs.* OF STANDARD ISP ADDED USING ELECTRODE (2-HEMA+DVB+DBS)

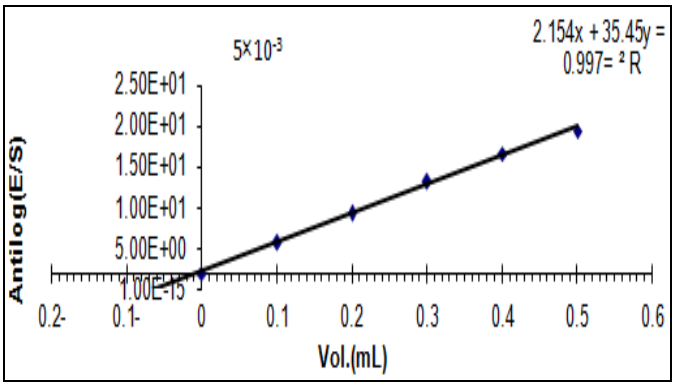

FIG. 22: VARIATION OF ANTILOG (E/S) OF SYNTHETIC SOLUTION OF 5× 10^{-3} M *vs.* OF STANDARD ISP ADDED USING ELECTRODE (2-HEMA+DVB+DBS)

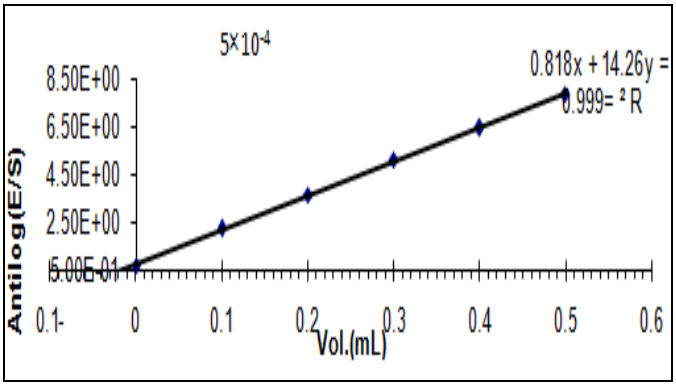

FIG. 23: VARIATION OF ANTILOG (E/S) OF SYNTHETIC SOLUTION OF 5×10^{-4} M *vs.* OF STANDARD ISP ADDED USING ELECTRODE (2-HEMA+DVB+NB)

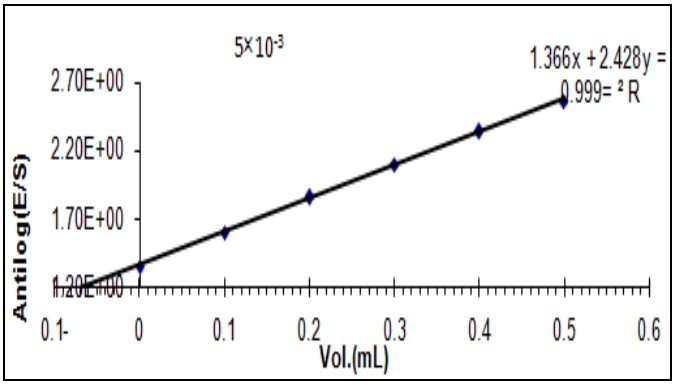

FIG. 24: VARIATION OF ANTILOG (E/S) OF SYNTHETIC SOLUTION OF 5×10^{-3} M *vs.* OF STANDARD ISP ADDED USING ELECTRODE (2-HEMA+DVB+NB)

A typical plot for membrane IT and IIIT at a concentration of synthetic solution (5×10^{-3}, 5×10^{-4}) M is shown in **Fig. 17-24** and the standard solution added was 0.1 M.

TABLE 6: RESULTS OF RECOVERY AND STANDARD DEVIATION OF COMMERCIAL DRUGS OBTAINED BY USING MEMBRANE IT, IIIT

Pharmaceutical Drug	Electrode No.	Potentiometric methods	Concentration Prepared/ M	Concentration Found/ M	% Rec.	% RE	% RSD
Samara-Salabid 5 mg	IT	Direct method	5.0×10^{-3}	5.0565 ×10^{-3}	101.13	1.13	2.26
		SAM		4.9384 ×10^{-3}	98.77	-1.23	1.15
		Direct method	5.0×10^{-4}	4.91098×10^{-4}	98.22	-1.78	1.56
		SAM		4.926610^{-4}	98.54	-1.46	1.81
Samara-Salabid 5 mg	IIIT	Direct method	5.0×10^{-3}	5.0753×10^{-3}	101.50	1.50	1.75
		SAM		4.9837×10^{-3}	99.68	-0.32	1.43
		Direct method	5.0×10^{-4}	5.0215×10^{-4}	100.43	0.43	2.75

		SAM		5.1002×10^{-4}	102.004	2.004	2.31
Ajanta Pharma-Isopropamide 5mg	IT	Direct method	5.0×10^{-3}	5.0628×10^{-3}	101.25	1.25	2.25
		SAM		4.9485×10^{-3}	98.97	-1.03	1.16
		Direct method	5.0×10^{-4}	$5.0912\ x10^{-4}$	101.82	1.82	2.71
		SAM		5.0627×10^{-4}	101.25	1.25	2.31
Ajanta Pharma-Isopropamide 5mg	IIIT	Direct method	5.0×10^{-3}	5.084610^{-3}	101.69	1.69	1.51
		SAM		5.0735×10^{-3}	101.47	1.47	2.32
		Direct method	5.0×10^{-4}	4.9221×10^{-4}	98.45	-1.55	1.95
		SAM		5.0973×10^{-4}	101.95	1.95	1.18

Direct method and standard additions method (SAM) was applied for the determination of Isopropamide in commercial pharmaceutical tablets (Salabid 5 mg, Isopropamide 5 mg) obtained from local stores using membrane IT, IIT, IIIT, and IVT. The values of the % recovery **Table 6**, **7** 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 the standard additions method were in good agreement with the results of the direct method.

CONCLUSION: The construction of molecularly imprinted electrodes sensors (MIP) using Isopropamide as a template and divinylbenzene (DVB) as cross-linkers and (2-vinyl pyridine (2V-P), and 2-hydroxyethyl methacrylate (2-HEMA) as monomers 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 DBS and NB plasticizers. Good results of recoveries were obtained for the determination of Isopropamide in the commercial tablets in comparison with the British Pharmacopoeia.

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CONFLICT OF INTEREST: Nil

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