RESEARCH ARTICLE

Preparation of New Molecularly Imprinted Polymers and its Use in the Selective Extraction For Determination Phenylephrine Hydrochloride at Pharmaceuticals

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ABSTRACT

This study was aimed at four electrodes were synthesized based on molecularly imprinted polymers (MIPs). Two MIPs were prepared by using phenylephrine hydrochloride (PPH) as the template, methyl methacrylate (MMA) as monomer as well as trimethylol propane tri methacrylate (TMPTMA) and ethylene glycol dimethacrylate (EGDMA) as cross linkers respectively and benzoyl peroxide as initiator. The same composition was used in the preparation of non-imprinted polymers (NIPs), but without the template (Phenylephrine hydrochloride). For the preparation of membranes, different plasticizers were used in the PVC matrix, such as Dioctyl phthalate (DOPH), dibutyl phthalate (DBPH), and nitrobenzene (NB). The characteristics studied are the slop, detection limit, lifetime, and linearity range of PPH–MIPs electrodes. Results obtained from selectivity measurements on interfering cations (K^+, Ca^{+2}, Al^{+3}) and some pharmaceutical additives such as methylparaben, propylparaben, trisodium citrate showed no interfering with drug phenylephrine hydrochloride. The preparation electrodes have been shown good response including testing pharmaceutical analysis.

Keywords: Different plasticizers, Molecularly imprinted electrodes, Phenylephrine hydrochloride, Potentiometric method, (MMA) monomer.

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INTRODUCTION

Phenylephrine hydrochloride [(1R)-1-(3-Hydroxyphenyl)-2-(methylamino) ethanol hydrochloride].[1] Phenylephrine hydrochloride is a white or almost white, crystalline powder, freely soluble in water and in ethanol (96 percent).[2] Phenylephrine hydrochloride indications can be used in severe hypotension, treat tachycardia although it is not a first-line drug, combined with isoprenaline which acts a bronchodilator if taken as inhaled drug, treatment of nasal congestion and cough, treatment of priapism, as a mydriatic drug, aids in diagnosis, treatment of eye diseases, treatment of upper respiratory tract infections, sinusitis, flu and tearful eyes.[3] Phenylephrine hydrochloride's side effects can cause extreme vasoconstriction and elevate blood pressure, tachycardia, or bradycardia. This drug should be avoided in patients with thyroid disease, heart disease, and anemia, contraindicated in patients, which enlarged prostate and diabetes, there are case reports of conjunctivitis in patients who have used PPH drops without medical prescription, and there was one case study of a patient hallucinating after using inhaled medication containing 0.5% of PPH.[4] The chemical formula of phenylephrine hydrochloride is $C_9H_{13}NO_2$.HCl, (M.Wt.:203.7 $g.mol^{-1}$) and its structural formula is shown in Figure. 1.

According to review, phenylephrine hydrochloride was determination by several methods such as these recent spectrophotometry,[5] spectrophotometry method for estimating infinitesimal amounts of phenylephrine hydrochloride,[6] HPLC reversed-phase technique,[7] HPLC technique,[8] liquid chromatography technique,[9] thin layer chromatography technique,[10] voltammetric differential Pulse Method,[11] capillary electrophoresis method,[12] combining liquid chromatography and mass spectrometry techniques and comparing results with HPLC-UV,[13] micellar electrokinetic chromatography

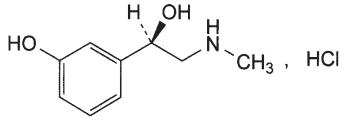

Figure 1: Structure of phenylephrine hydrochloride

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method.[14] Several techniques used for determination drugs and pharmaceuticals. The selective electrodes technique one of these techniques used for determination phenylephrine hydrochloride because this technique has many characteristics like fast response time, easy used, rapid, low cost, and selectivity. The potentiometric sensors techniques that are based on PVC membranes electrodes widely available used for the analysis of drugs and ionic species.[15-17] MIPs were used the phenylephrine hydrochloride as the template. In contrast, the monomer, which was used in MM as well as TMPTMA and EGDMA as cross-linkers, respectively and benzoyl peroxide as an initiator to achieved the polymerization process. There is a variety of ion-selective electrode determined drugs that depended on MIP_S as recognition membranes like diclofenac sodium,[18] warfarin,[19] phenytoin,[20] and metronidazole benzoate.[21] This study used different plasticizers to the construction of membranes electrodes based on PPH-MIP_S, such as dioctyl phthalate (DOPH), dibutyl phthalate (DBPH), and nitrobenzene (NB).

MATERIALS AND METHODS

Preparation of Molecularly imprinted polymer (MIP) and non-imprinted polymer (NIP)

For preparation first phenylephrine hydrochloride molecularly imprinted polymer (PPH-MIP1), 0.45 mmol (0.09 g) from phenylephrine hydrochloride then mixed with 3.60 mmol (0.36 g) methyl methacrylate as the monomer, after that added 11.00 mmol (3.72 g) trimethylol propane tri methacrylate to the solution as the crosslinker, followed that added 0.32 mmol (0.07 g) benzoyl peroxide as the initiator. All these materials were dissolved in 5 ± mL methanol (CH_3OH). While the second PPH-MIP2 were achieved by mixed 0.60 mmol (0.12g) from phenylephrine hydrochloride as the template, 4.00 mmol (0.40g) methyl methacrylate as the monomer, 20.00 mmol (3.96g) ethylene glycol dimethacrylate as the cross-linker and 0.36 mmol (0.08 g) benzoyl peroxide as the initiator which dissolved in 5 ± mL of methanol (CH_3OH). For obtaining a homogeneous solution, the mixture was stirred for 5 minutes. N_2 passes for 30 minutes on the mixture to remove oxygen from the solution. After that, the solution was placed in a water bath at 60℃. when the reaction completes the molecularly imprinted polymer became hardened, after the polymerization process, the polymer was drying and crashed to obtain a polymer particle. These particles were sonicated in CH_3OH/CH_3COOH (30:3 v/v) to remove the template from MIP. The particle size of PPH-MIP1 and PPH-MIP2 were between 43–60 µm and 75-125µm, respectively. The preparation of non-molecularly imprinted polymers using the same substances and conditions that formed PPH-MIP1 and PPH-MIP2 but without the phenylephrine hydrochloride (template). The same composition was used in the preparation of non-imprinted polymers (NIPs), but without the template (Phenylephrine hydrochloride).

Instruments

Ion analyzer used in this work (WTW model, Germany), a pH meter (WTW model pH 720, Germany), and a saturated calomel electrode (Gallenkamp, USA). The electrode PPH-MIP used was construction in the laboratory, and all potentiometric measurements were made at room temperature. The phenylephrine hydrochloride-MIP electrode combined with the Ag-AgCl electrode, and the reference electrode was 0.1 M internal solution of phenylephrine hydrochloride. The PVC tube (1-4 cm long) was flattened and polished by putting it on a glass plate and soaking with THF. The membrane was cut similar to the external diameter of the PVC tubing and pasted on the polished end. The other direction of the PVC tubing was then linked to the electrode body. To make the electrodes more sensitive was by soaking in 0.1 M bromhexine hydrochloride solution for at least (2-3 hours) before the use of the electrodes.

Materials and chemicals

- Standard phenylephrine hydrochloride obtained from industries of pharmaceuticals (IRAQ-SDI -Samarra). NASOPHRINE 10mL 0.25% from (SDI -Iraq), phenylephrine/cooper 10mL 5% from (Kooper.gr-Germany), Nasophrine 10mL 0.5% from (Sina-darou-Iran) were purchased from local pharmacies.
- Plasticizers, dioctyl phthalate (DOPH) (99.5% purity), dibutyl phthalate (DBPH) (98.0% purity), and nitrobenzene (NB) (99.4% purity), were purchased from Sigma Aldrich. Other chemicals and reagents materials were obtained from Fluka, BDH and Sigma Aldrich.

Preparing of standard solutions

- For preparing a standard solution of 0.1 M phenylephrine hydrochloride by dissolving 1.0185 g of standard phenylephrine hydrochloride in methanol and completed to 50 mL in the volumetric flask. The other solutions were prepared in 25 mL at the ranged from 10^{-6}–10^{-1} M in the same procedure.
- The stock standard solution of 1×10^{-3} M, 1×10^{-4} M, phosphomolybdic acid was prepared by dissolving 0.225g, 0.022g, respectively in distilled water and completed to 100 mL.
- All interfering cations (K^+, Ca^{+2}, Al^{+3}) and some pharmaceutical additives such as methylparaben, propylparaben, trisodium citrate 0.1 M stock solution prepared at ranged from 10^{-6} - 10^{-1} M which present the interfering ions were prepared and diluted to 100 mL.

Synthesis of membrane molecularly imprinted polymers electrode

Phenylephrine hydrochloride membrane was immobilized into the PVC tube, as portrayed by Thomas and Moody.[15] PPH-MIP of 0.036g was mixed with different of plasticizers 0.4g used in this work such as DOPH (electrode A1), DBPH (electrode A2), NB (electrode B1) and DOPH (electrode B2). Then added 0.20g of PVC powder was scattered on 7 ± mL of tetrahydrofuran with stirring until a clear, viscous solution was acquired. Later the solutions mixed with stirring until the mixture became homogeneous. The mixture was casted into a glass ring 30-35 mm diameter and unwind on a glass plate and a ribbon of filter was placed on top of the glass.

The solvent was then allowed to evaporate according to room temperature more than 24–48 hours, at least. The thickness of the membrane obtained was different of the membrane to others; the thickness was about 0.4-0.7 mm. That size of the membrane was adequate to prepare electrodes.

Scanning electron microscope (SEM)

In scanning electron microscopy, a fine beam of electrons scans the membrane surface. This causes several kinds of interactions generating different signals, also used in image formation. The SEM can be used to get an idea about the size, geometry, and distribution of pore surface of the membranes. SEM analysis showed the highly ordered and regular pore structure of the molecular imprinted polymer surface and the cross-section. Several papers showed that the imprinted molecular membranes recognized the template molecule effectively and transported it with good efficiency due to porous structures of the molecularly imprinted polymer. The ordered porous and cross-section on the surface shows the sites of interaction, and MIP showed the highest transport rate towered the template molecule. The morphology of MIP before and after washing showed by electron microscope in Figure (2a, 2b) and Figure (3a, 3b). Microemulsion polymerization gives very small particles size around (1.100–1.400) Mm and (0.900–1.200)Mm for methyl methacrylate (MMA) polymer in both MIP_S can be distinguished in the related image.

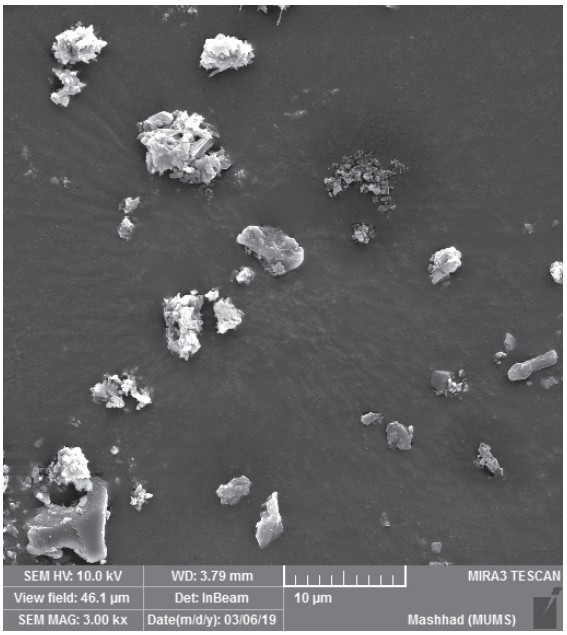


Figure 2a: SEM for the MIP1 before washing

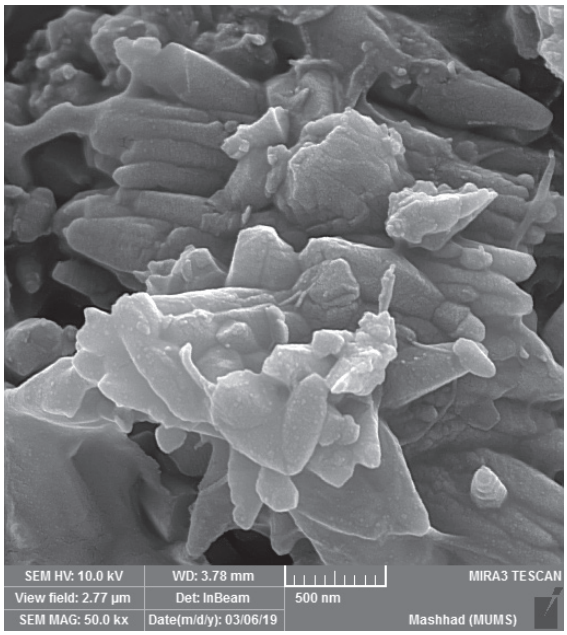


Figure 2b: Shows the SEM for MIP1after washing

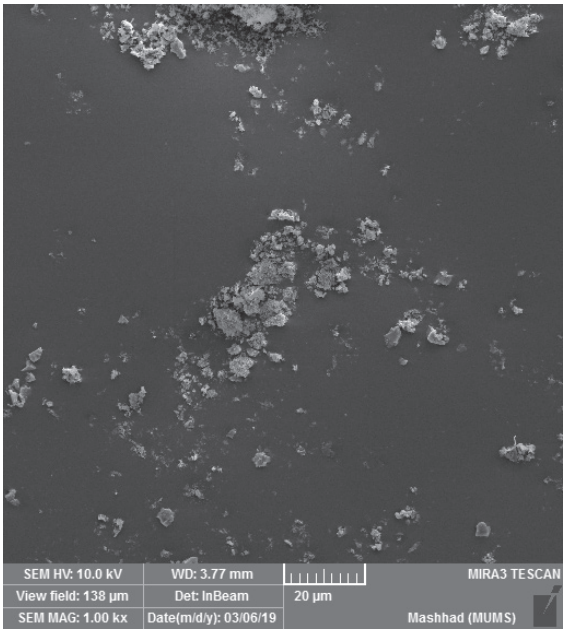


Figure 3a: SEM for the MIP2 before washing

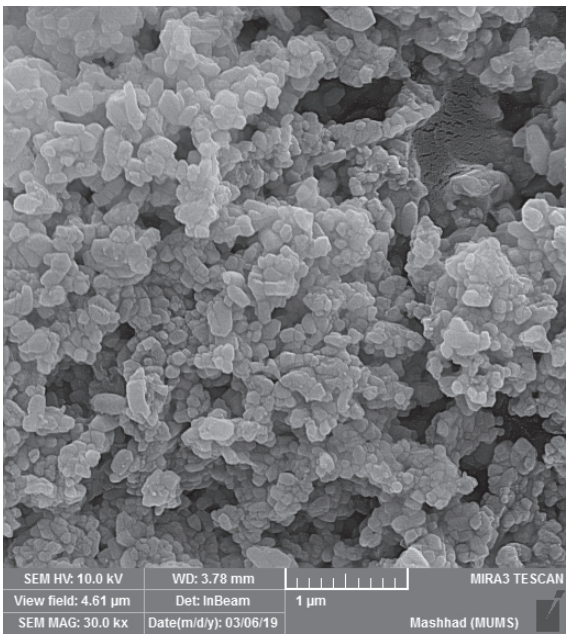


Figure 3b: Shows the SEM for MIP2 after washing

The morphology of the prepared membrane using the PPH-MIP1 before washing is shown in figure 2a and after washing is shown in Figure 2b. Figure 2a (before washing) reveals that the particles of the complex are formed in a regular spherical shape with an average of about μm in diameter. On the other hand, Figure 2b (after washing) shows that the formed particles look like a colloidal particle growing in a solution; this might take place due to the presence of an excess of DFS that form ionic atmosphere surrounding the complex and create the formation of electric double layers.

Construction of ion-selective electrodes

The building of the electrode body and the immobilization were achieved as portrayed by Mahajan *et al.*[22] phenylephrine hydrochloride solution (0.1) M was filled in the glass tube as an internal solution. Preferred immersing the membrane in a standard solution of (0.1) M of phenylephrine hydrochloride for at least (2 to 3) hours before measurements, which represents stipulations of membrane electrode.

Preparation of pharmaceutical samples

The contents of two bottles of eye drop and nasal drop (each bottle contains 5% and 0.25% of PPH for eye drops and nasal, respectively). A specific amount of these drops, which was equivalent to a stock solution with a concentration of about 10^{-3} M, was transferred into a 50 mL calibrated flask and completed to the volume with distilled water.

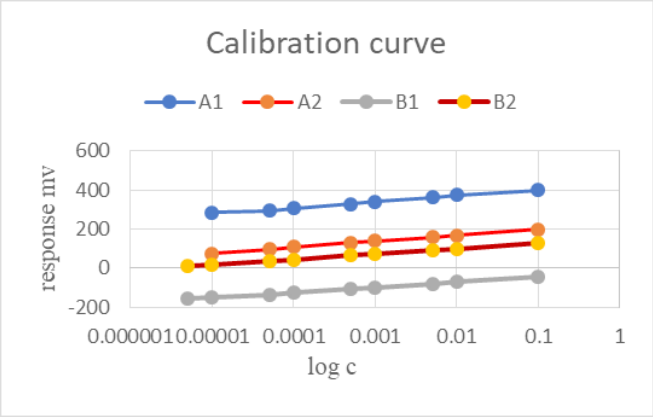


Figure 5: Calibration curve for PPH-MIP1 and PPH-MIP2 membranes electrodes

Two MIPs have been prepared by using the phenylephrine hydrochloride (PPH) as the template, methyl methacrylate (MMA) as monomer as well as tri methylolpropane tri methacrylate (TMPTMA) and ethylene glycol dimethacrylate (EGDMA) as cross linkers respectively and benzoyl peroxide as initiator. A plasticizer is an important component in an ISE membrane. Compatibility with the polymer and other membrane constituents provides a homogeneous environment for membrane when the plasticizers using as a solvent for the membrane practical use of ISE membrane should be avoided leaching of the plasticizer; otherwise, it would affect the electrode performance over time. Four electrodes have been constructed based on the PVC matrix, these plasticizers, such as Dioctyl phthalate (DOPH), DBPH and NB. The characteristics were studied for all electrodes based on PPH-MIP1 (A1, A2 membranes) and PPH-MIP2 (B1, B2 membranes), which included linearity range, correlation coefficients, detection limit (M) and lifetime (day) respectively. The results obtained showed in Table 1 and Figure 5.

Effect of pH on electrodes response

The study of pH effected on PPH membranes electrodes by prepared various concentrations of PPH (1×10^{-2}, 1×10^{-3} and 1×10^{-4}) M. To measurement the selective pH at ranged (1-11) by using the hydrochloric acid (0.1 M ,1 M) and/or sodium hydroxide (0.1 M,1 M) for pH studies. The results obtained by adding an appropriate volume of HCl/NaOH, as shown in Table 2 and Figure 6,7. The change in potentials at differential pH values may be due to the composition of electrodes. This composition also affects response and lifetime for electrodes.

Calculation by Multiple Standard Addition Method (MSA)

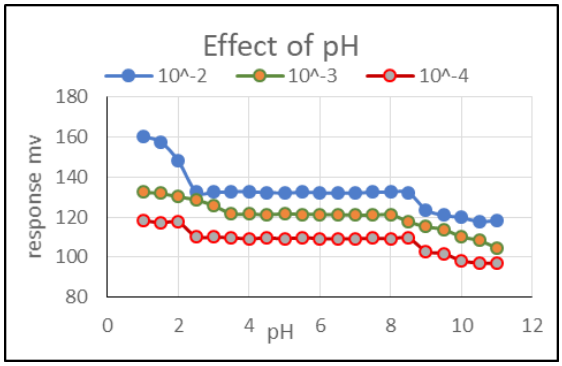
The concentrations used for applied in this method (1×10^{-3} & 1×10^{-4}) for two solutions of phenylephrine hydrochloride for plotting the antilog E/S (Y-axis) against volume of standard phenylephrine hydrochloride (X-axis). Figure (10, 11, 12 and 13) represents the results of phenylephrine hydrochloride

Table 1: Characteristics of the phenylephrine hydrochloride-MIP electrode based on different functional monomers and plasticizers.

Membrane composition	*PPH-MIP1 + DOPH (A1)*	*PPH-MIP1 +DBPH (A2)*	*PPH-MIP2 +NB (B1)*	*PPH-MIP2 +DOPH (B2)*
Slop (mV/decade)	30.30	30.60	26.60	28.19
Linearity range (M)	1×10^{-5}-1×10^{-1}	1×10^{-5}-1×10^{-1}	5×10^{-6}-1×10^{-1}	5×10^{-6}–1×10^{-1}
Correlation coefficient	0.9928	0.9989	0.9977	0.9989
Detection limit (M)	5.6×10^{-6}	5.3×10^{-6}	4.7×10^{-6}	3.4×10^{-6}
Life time (day)	25	18	8	21

Table 2: Working pH range for Phenylephrine Hydrochloride Selective electrode

Number and composition of MIPs	*Membranes*	*Membrane composition*	*pH range*		
			1×10^{-2}M	*1×10^{-3}M*	*1×10^{-4}M*
MIP1	A1	PPH-MIP1 +DOPH	2.5–8.5	3.5–8.0	3.5–9.0
PPH+MMA+ TMPTMA	A2	PPH-MIP1 +DBPH	3.5–9.0	3.0–6.5	4.0–9.0
MIP2					
PPH+ MMA+	B1	PPH-MIP2+NB	3.5–7.5	3.0–8.0	2.0–7.0
EGDMA	B2	PPH-MIP2 +DOPH	3.5–9.5	2.5–7.5	3.5–8.0



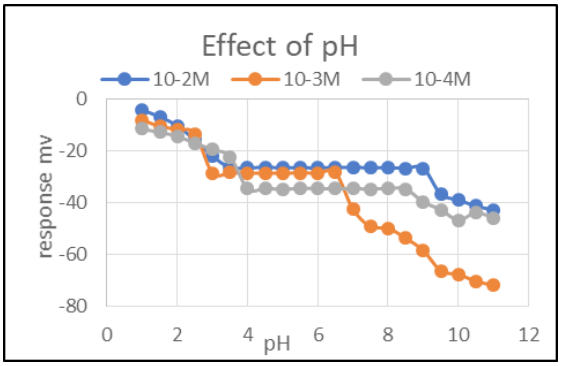
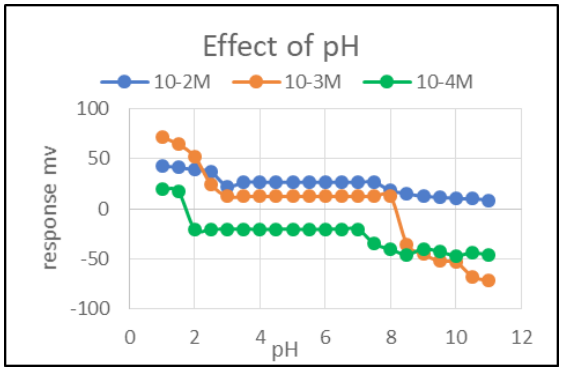


Figure 6: Effect of pH on the Phenylephrine Hydrochloride {PPH-MIP1 + DOPH (A1) and PPH-MIP1 +DBPH (A2)} electrodes at concentration 1×10^{-2}, 1×10^{-3} and 1×10^{-4}M.



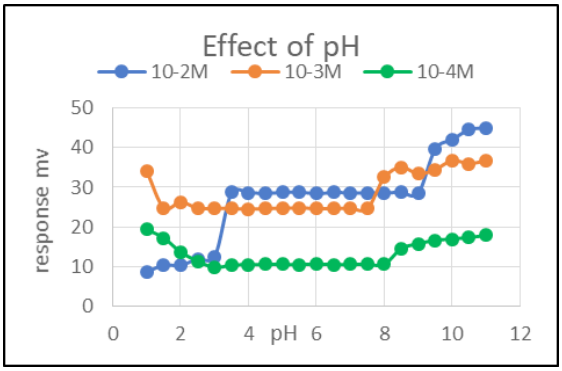
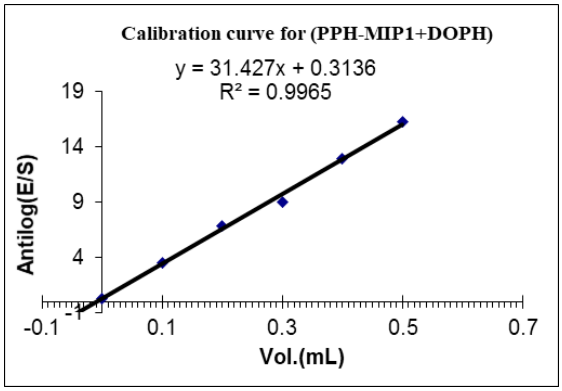


Figure 7: Effect of pH on the Phenylephrine Hydrochloride {PPH-MIP2 + NB (B1) and PPH-MIP2 +DOPH (B2)} electrodes at concentration 1×10^{-2}, 1×10^{-3} and 1×10^{-4}M.



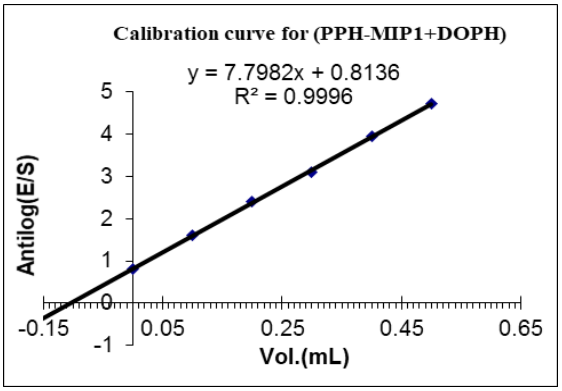
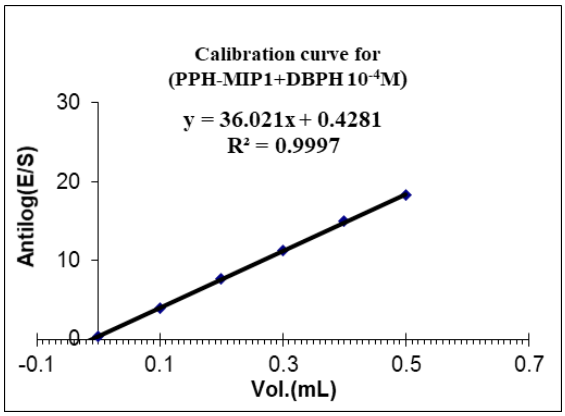


Figure 10: Antilog (E/S) against the volume of the added standard for the determination of phenylephrine hydrochloride solution (1×10^{-3} and 1×10^{-4}) by MSA using (PPH–MIP1 + DOPH) electrode



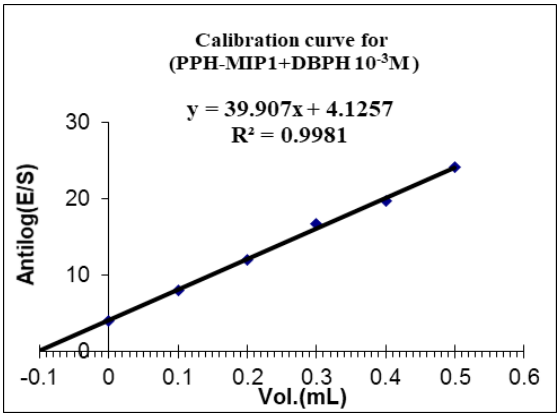


Figure 11: Antilog (E/S) against the volume of the added standard for the determination of phenylephrine Hydrochloride solution (1×10^{-3} and 1×10^{-4}) by MSA using (PPH–MIP1 + DBPH) electrode.

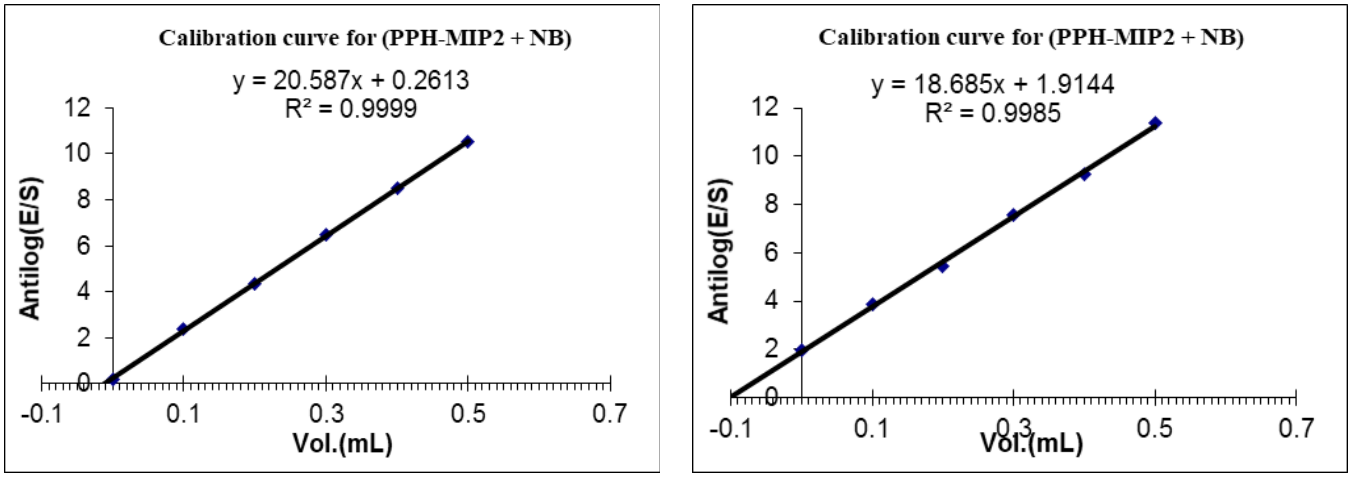


Figure 12: Antilog (E/S) against the volume of the added standard for the determination of phenylephrine Hydrochloride solution (1×10^{-3} and 1×10^{-4}) by MSA using (PPH–MIP2 +NB) electrode.

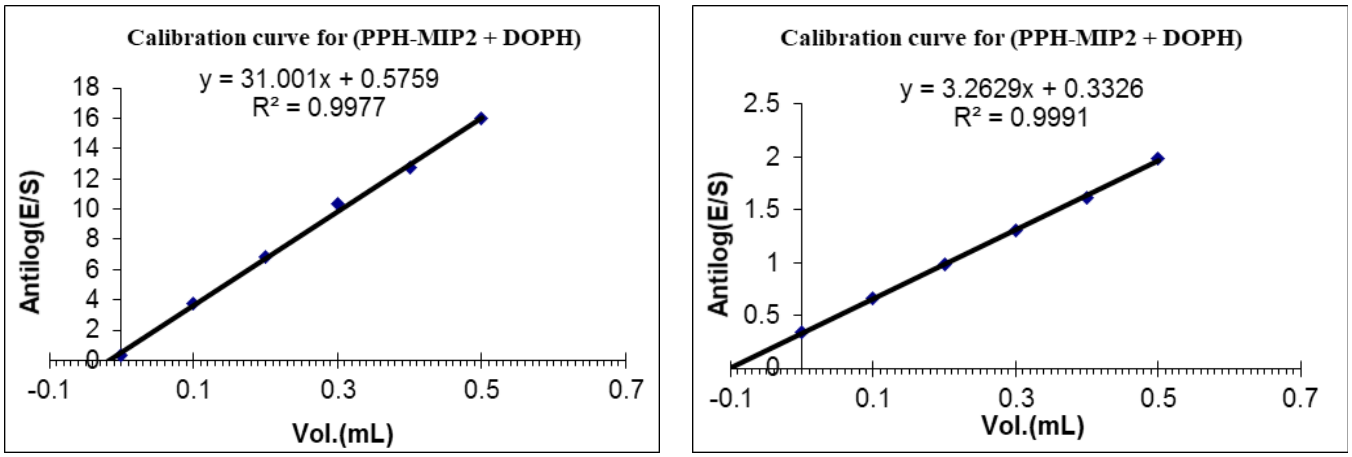


Figure 13: Antilog (E/S) against the volume of the added standard for the determination of phenylephrine Hydrochloride solution (1×10^{-3} and 1×10^{-4}) by MSA using (PPH–MIP2 +DOPH) electrode.

concentrations calculated via the electrodes based on PPH-MIP1+ DOPH, PPH-MIP2+DOPH.

Titration methods (Titrimetry)

In this method, the measurement is depended on changes that to be a large shift in the electrode response for the detection of the end point of titration. The process has been achieved by used volumetric analysis of concentrations (1×10^{-3} and 1×10^{-4}) M of phenylephrine hydrochloride versus solutions (1×10^{-3} and 1×10^{-4}) M of concentrations (PMA). The results for the parameter RSD%, RC%, and RE% for all electrodes are listed in Table 7.

Applications of pharmaceuticals

Ion-selective electrodes that based on molecularly imprinted polymers were used for the determination of phenylephrine

Table 7: Phenylephrine hydrochloride sample analyses by using titration method for PPH electrodes

Electrode No.	Concentration (M)	
PPH – MIP_1 + DOPH (1)	Sample	Measured using PMA as titrant
	1×10^{-3}	1.0423×10^{-3}
	RSD%	1.6082 & 1.44245
	RC%	103.95
	RE%	3.95
	1×10^{-4}	1.0341×10^{-4}
	RSD%	2.756 & 1.9939
	RC%	102.89
	RE%	2.89
Electrode No.	Concentration (M)	

Cont.

Cont.

PPH – MIP_1 + DBPH (2)	Sample	Measured using PMA as a titrant
	1×10^{-3}	1.036×10^{-3}
	RSD%	1.366904&1.3980
	RC%	103.633
	RE%	3.633
	1×10^{-4}	1.030×10^{-4}
	RSD%	2.0905&1.64472
	RC%	103.33
	RE%	3.33
Electrode No.	Concentration (M)	
PPH – MIP2 + NB (1)	Sample	Measured using PMA as titrant
	1×10^{-3}	1.025×10^{-3}
	RSD%	0.918365&0.88229
	RC%	102.533
	RE%	2.533
	1×10^{-4}	1.03×10^{-4}
	RSD%	0.795289&0.800227
	RC%	102.66
	RE%	2.66
Electrode No.	Concentration (M)	
PPH – MIP2 + DOPH (2)	Sample	Measured using PMA as titrant
	1×10^{-3}	1.035×10^{-3}
	RSD%	1.386734&1.406265
	RC%	103.5
	RE%	3.5
	1×10^{-4}	1.04×10^{-4}
	RSD%	2.083839&2.493658
	RC%	103.66
	RE%	3.66

hydrochloride in pharmaceuticals. This ISEs measurement, including standard addition, direct, Gran plot, and multiple standard addition method. Preparation solutions of phenylephrine hydrochloride at concentrations $1\times10^{-3}$and 1×10^{-4} M.The RE%, RC% and RSD% were calculated of phenylephrine hydrochloride in pharmaceuticals. The results obtained represented in the Table (8, 9, 10, and 11).

CONCLUSION

Phenylephrine hydrochloride membranes selective electrodes can be constructed by mixing with different plasticizers. These plasticizers DOPH, DBPH, and NB, were used to prepared phenylephrine hydrochloride membranes electrodes based on PVC. The results obtained for all electrodes were excellent as well as applied to standard and pharmaceutical solutions.

Table 8: Sample Analysis of pharmaceuticals phenylephrine hydrochloride by using ISE.

	NASOPHRINE 0.25% (Samarra) by MIP1+DOPH			
Pharmaceutical	*Direct method*	*SAM*	*MSA*	*Titration method*
Concentration prepared	1×10^{-3}	1×10^{-3}	1×10^{-3}	1×10^{-3}
*Found	0.9726×10^{-3}	1.0143×10^{-3}	1.0097×10^{-3}	1.049×10^{-3}
REC%	97.26	101.43	100.97	104.87
RE%	-2.74	1.43	0.97	4.87
*RSD%	0.1349	0.06	-------	1.893
F experimental	5.25	1.56	-------	2.08
F theoretical	19.2			
Pharmaceutical	NASOPHRINE 0.25% (Samarra) by MIP1+DOPH			
	Direct method	SAM	MSA	Titration method
Concentration prepared	1×10^{-4}	1×10^{-4}	1×10^{-4}	1×10^{-4}
*Found	0.9831×10^{-4}	0.9876×10^{-4}	1.0108×10^{-4}	1.030×10^{-4}
REC%	98.31	98.77	101.08	103.26
RE%	-1.69	-1.23	1.08	3.26
*RSD%	0.1892	0.09	-------	1.568
F experimental	8.58	2.33	-------	6.25
F theoretical	19.2			

Table 10: Sample Analysis of pharmaceuticals phenylephrine hydrochloride by using ISE.

	NASOPHRINE 0.25% (Samarra) by MIP2+NB			
Pharmaceutical	*Direct method*	*SAM*	*MSA*	*Titration method*
Concentration prepared	1×10^{-3}	1×10^{-3}	1×10^{-3}	1×10^{-3}
*Found	0.9754×10^{-3}	1.0229×10^{-3}	1.0176×10^{-3}	1.029×10^{-3}
REC%	97.54	102.29	101.76	102.9
RE%	-2.46	2.29	1.76	2.90
*RSD%	-0.4452	-0.31	-------	2.258693
F experimental	4.75	1.57	-------	1.56
F theoretical	19.2			
Pharmaceutical	NASOPHRINE 0.25% (Samarra) by MIP2+NB			
	Direct method	SAM	MSA	Titration method
Concentration prepared	1×10^{-4}	1×10^{-4}	1×10^{-4}	1×10^{-4}
*Found	1.0303×10^{-4}	0.97603×10^{-4}	0.97627×10^{-4}	1.040×10^{-4}
REC%	103.03	97.60	97.63	103.66
RE%	3.03	-2.40	-2.37	3.66
*RSD%	-0.2032	-0.19	-------	1.279513
F experimental	1.58	3.12	-------	6.25
F theoretical	19.2			

Table 11: Sample Analysis of pharmaceuticals phenylephrine hydrochloride by using ISE.

	NASOPHRINE 0.25% (Samarra) by MIP2+DOPH			
Pharmaceutical	*Direct method*	*SAM*	*MSA*	*Titration method*
Concentration prepared	1×10^{-3}	1×10^{-3}	1×10^{-3}	1×10^{-3}
*Found	1.0211×10^{-3}	1.0205×10^{-3}	1.0119×10^{-3}	1.03×10^{-3}
REC%	102.11	102.05	101.19	103.0
RE%	2.11	2.05	1.19	3.0
*RSD%	0.28386	0.17	--------	1.248249
F experimental	1.56	3.12	-------	4.46
F theoretical	19.2			
Pharmaceutical	NASOPHRINE 0.25% (Samarra) by MIP2+DOPH			
	Direct method	SAM	MSA	Titration method
Concentration prepared	1×10^{-4}	1×10^{-4}	1×10^{-4}	1×10^{-4}
*Found	0.9743×10^{-4}	0.98212×10^{-4}	0.98927×10^{-4}	1.03×10^{-4}
REC%	97.43	98.21	98.93	103.0
RE%	-2.57	-1.79	-1.07	3.0
*RSD%	0.12955	0.11	-------	2.521653
F experimental	6.25	6.25	-------	1.56
F theoretical	19.2			

Table 9: Sample Analysis of pharmaceuticals phenylephrine hydrochloride by using ISE.

	NASOPHRINE 0.25% (Samarra) by MIP1+DBPH			
Pharmaceutical	*Direct method*	*SAM*	*MSA*	*Titration method*
Concentration prepared	1×10^{-3}	1×10^{-3}	1×10^{-3}	1×10^{-3}
*Found	0.9865×10^{-3}	0.98784×10^{-3}	0.98889×10^{-3}	1.044×10^{-3}
REC%	98.65	98.78	98.89	104.43
RE%	-1.35	-1.22	-1.11	4.433
*RSD%	0.2535	0.12	-------	2.609
F experimental	3.08	1.56	-------	1.25
F theoretical	19.2			
Pharmaceutical	NASOPHRINE 0.25% (Samarra) by MIP1+DBPH			
	Direct method	SAM	MSA	Titration method
Concentration prepared	1×10^{-4}	1×10^{-4}	1×10^{-4}	1×10^{-4}
*Found	0.9802×10^{-4}	0.9882×10^{-4}	0.98991×10^{-4}	1.02×10^{-4}
REC%	98.018	98.82	98.99	102.333
RE%	-1.981	-1.18	-1.01	2.333
*RSD%	0.70218	4.55&0.36	-------	1.5922
F experimental	12.25	8.58	-------	3.12
F theoretical	19.2			

The aim of construction electrodes for used in determination phenylephrine hydrochloride in pharmaceuticals analysis.

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