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New Ion Selective Electrodes for Analysis of Metformin Based on Molecularly Imprinted Polymers

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Abstract

Metformin (MEF) imprinted polymer liquid electrodes are created using a precipitation polymerization process. The MEF served as a template for the creation of molecularly imprinted (MIP) materials using benzoyl peroxide (BPO) as an initiator, allyl methacrylate (AMA) crosslinkers, and glycidyl methacrylate (GMA) as a monomer. Utilizing Di-octyl-phthalate (DOPH) and di-butyl phthalate (DBPH) as plasticizers in a PVC matrix, the molecularly imprinted membranes are created. The reaction time is approximately 50 seconds, and the limits of detection for liquid electrodes, as determined by the calibration curves, are 55.6 to 58.4 mV/decade at 5×10^{-5} M and 8×10^{-5} M respectively. The liquid electrodes demonstrated good selectivity over a variety of species and a consistent reaction when filled with a typical 0.1 M drug solution across the pH range of 1 to 11. Modern electrodes can detect MEF without the need for time-consuming pre-treatment procedures in pharmaceutical samples.

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1. Introduction

A promising technique for creating binding receptor sites that are specifically created by rearranging templates and functional monomers is called molecularly impressed polymers (MIPs) [1-4]. Functional monomers and crosslinkers create cavities in which the model is inserted when template molecules are present. By forming a hydrogen bond A functional monomer, In the first step, the template is in contact with the electrostatic interactions, van der Waals forces, and reversible covalent bonds. The combination of monomer and template is then polymerized in a subsequent phase while being exposed to a considerable amount of excess cross-linking agent [5-7]. The functional monomer model can be accommodated by the cross-linkers and the monomer's chemical connections. After polymerization, the template can be removed, revealing binding sites with new forms, sizes, and chemical characteristics [8-11]. A biguanide antihyperglycemic drug is metformin. It functions by reducing the amount of glucose produced by the liver, improving the body's tissues' sensitivity to insulin, and raising the release of GDF15 (growth differentiation factor, a protein-coding gene), which suppresses hunger and calorie intake [12-15]. The metformin structure is depicted in Figure 1 [16]. In this work identifies the preparation of MIP with recognition cites MIP allyl methacrylate (AMA) crosslinkers, and glycidyl methacrylate (GMA) as a monomer. With benzoyl peroxide, BPO is an initiator for the target molecule Metformin. SEM and FTIR were used to characterize the prepared MIPs. In addition, solid phase extraction

and initial Metformin concentration, on adsorption capacity were studied.

2. Experimental Details

2.1. Instrumentation

The JSM.6390A scanning electron microscope (JSM.6390A) (TOKYO JAPAN), the FTIR Shimadzu (FTIR)-8000 (Japan), heating/stirring (Germany), centrifuge (Germany) and vacuum pump were employed in addition to the Wissenschaftlich-TechnischeWerkstätten GmbH WTW/pH meter in lab pH720-Germany to measure pH.

2.2. Chemicals

Merck (Darmstadt, Germany) provided the metformin Samarra Iraq, methanol, nitrogen gas (99.99), chloroform, and acetic acid. Sigma-Aldrich was used to purchase the di-octyl phthalate (DOPH) and dibutyl phthalate (DBPH) and for the metal salts. Sigma-Aldrich supplied the (allyl methacrylate) (AMA) (99%), (glycidyl methacrylate) (GMA) (99%), and benzoyl peroxide (BPO) (78%). All the chemicals in the present work are extremely pure and did not require further purification.

2.3. Imprinted polymer (MIP) synthesis

By using a bulk polymerization technique, MIP was created. For 5 minutes it was dissolved in 10 mL of chloroform and 0.0687 g (0.333) mmol (MEF) in a 50 mL thick-walled glass tube. 0.025 gm (0.1 mmoles) of BPO was combined with the initiator with 0.5684 g (4 mmol) glycidyl methacrylate and 2.0176 g (16 mmol) allyl methacrylate to generate the first MIP. The mixture was combined for 10 to 20 minutes in an ultrasonic water bath while being purged with nitrogen gas. To begin the reaction, the tube was put in a water bath that was heated to 55 degrees Celsius after it had been sealed for 30 minutes. MIPs were routinely washed with 100 mL sections of a 20% (v/v) acetic acid/methanol solution. For (24–72) hours, the polymers were pounded and mashed in a mortar and pestle at (30–40 °C). After drying at room temperature, they served as the active ingredient in the selective sensor membrane after being sieved to a particle size of 125 m (using a 100 mesh sieve). Like the prototype, the non-printed polymer (NIP) wasn't made using any drugs. PVC (0.2g, total molecular weight) These are mixed with plasticizer (0.045g) and MIP (0.036g). They added THF (4-5 mL) after homogenising the solution with stirring. The mixture was poured into a glass jar with a 5 cm diameter and a glass sheet shape. To allow the liquid to evaporate over 24 hours, a circular portion was added. The glass tube containing a silver wire covered in silver chloride and a 0.1 M normal metformin solution held the opposite end of the Tygon tube in place. The opposite end of the Tygon tube was securely fastened to the glass tube. For the electrode growth, a circular PVC membrane disc with a diameter of 10 mm was created using a concentrated PVC/THF solution as an adhesive. The particle shape and architecture were studied using a scanning electron microscope (SEM). Following washing a porous surface, electron microscopy shows the shape of the MIP and NIP membranes for metronidazole benzoate figure 2 (A). The binding faces of the polymer can be seen at a distance of around 20 m. Transparent holes with a 50 m diameter have been bored, as shown in figure 2 (B).

2.4. Potential Measurements

Measurements were made in a 50 mL double-walled glass cell under laboratory conditions while being magnetically stirred to produce a homogeneous solution. The effectiveness of the electrodes was evaluated through sequential dilution by determining the potential of commercially available pharmaceutical solutions prepared at concentrations between 101 and 106 M. The slope's operational lifetime, detection limit, and response time were determined using the calibration curve.

2.5. Pharmaceutical Sample Preparation

Pharmaceutical samples were prepared by grinding ten tablets and dissolving them in 1 M HCl in a 100 ml volumetric flask. Methanol was added agitated and warmed using a magnetic stirrer for at least 30 minutes. The solution was poured through cellulose filter paper 0.07µm, thereby securing concentrations 7×10^{-4} mmol/ml (0.7 µmol/ml), 1×10^{-4} mmol/mL (0.1 µmol/ml) (Daonil 5 mg / France, Glibesyn 5mg/Cyprus),

which have lowest standard addition (SD) value. It was subsequently used with MIP in a solid phase extraction (SPE) column.

3. Results and Discussion

3.1. Liquid Membranes Electrode

The range of concentrations of MIP-dependent liquid electrodes and the reaction of their slopes to the Nernstian equation were studied. Two plasticizers, DOPH and DBPH, are used in MIP membranes, which are made of (glycidyl methacrylate) (GMA),(allyl methacrylate) (AMA), and a PVC matrix. For all liquid electrodes, an internal solution of 0.1 M aqueous standard drug solution was utilised. Experimental results of molecularly impressed (MIP) synthesis based on (glycidyl methacrylate) (GMA) and (allyl methacrylate) (AMA), can be used to prepare successful MEF-MIP. The plasticizer, a crucial component of the sensing membrane, plays a critical role in regulating the mobility of the analyte inside the membrane and acting as a solvent for the various components. Making MEF electrodes based on MIP is appropriate for the two plasticizers DOPH and DBPH that were used. Table 1 displays the properties of the created and examined electrodes. Dioctylphthalate (DOPH), Dibutylphthalate (DBPH), and two other viscosity plasticizers were used to make four distinct compositional membranes, and the calibration curves produced the electrode specification results that are presented in Table 1. The linear dynamic ranges were from $1 \times 10^{-6} - 0.1\,M$, while the electrode slopes ranged between 55.6 and 58.4 mV/decade. The preparation's electrodes typically have a finite reaction time of 50 seconds or less. primarily at high concentrations. The values in Table 1 also show that the electrodes I MEF and II MEF performed well, therefore both drugs in pharmaceutical samples were determined using the liquid electrode.

3.2. Quantitative analysis

Using the usual addition method to measure metformin in synthetic solutions of 10^{-3} and 10^{-4} M, the accuracy of electrodes I through II was evaluated. Excellent percentage recovery results were attained between 96 and 101.9.% Figures 3 and 4 depict typical curves at a synthetic solution concentration for membranes I to II (10^{-3} M) with 0.1 M of standard solution added.

To determine the presence of metformin (Daonil 5mg/France, Glibesyn 5mg/Cyprus) in commercial pharmaceutical tablets, the direct technique and standard addition method were obtained by membranes from local Tables 1 and 2 that use DBPH and DOPH as plasticizers, respectively. The percentage recovery figures in Tables 2 and 3 line up with the value listed in the British Pharmacopoeia [17-18]. Since no species interferes with the electrode response, the recovery values obtained using the usual addition approach are consistent with the outcomes of the direct method.

4. Conclusions

Metformin (MEF) is used as a template, together with (allyl methacrylate) (AMA) as cross-linkers and (glycidyl methacrylate) (GMA) as monomers in various plasticizers, to create sensors for molecularly imprinted electrodes (MIP). Results of MIP Electrodes have been applied across a broad pH spectrum to achieve excellent sensitivity, fair selectivity, quick static response, long-term stability, and applicability plasticizers DBPH and DOPH. For the determination of metformin (MEF) in commercial tablets, good recovery values were observed when compared to the British Pharmacopoeia.

Table1. MEF-MIP electrode parameter based on various plasticizers

Electrode No.	Membrane composition	Parameter				
		Slope mV/decade	Correlation Coefficient (r)	Range of linearity M	Limit of detection (M)	Life time (day)
I	MEF-(MIP +DOPH)	55.6	0.9996	$1\times(10^{-6}\text{-}10^{-1})$	5×10^{-5}	25
II	MEF-(MIP+DBPH)	58.4	0.9994	$1\times(10^{-6}\text{-}10^{-1})$	8×10^{-5}	15

Table2. Results of commercial drug recovery and standard deviation calculated utilizing membrane I MEF - (MIP +DOPH)

Pharmaceutical Drug	Potentiometric methods	Prepared for Concentration / M	Concentration ($\times10^{-4}$M)	%Rec.	%RE	%RSD
Daonil 5mg	DM	1.0×10^{-4}	0.96	96	-4	0.36
	SAM		1.019	101.9	1.9	0.44
	DM	1.0×10^{-3}	0.0998	99.8	-0.2	0.92
	SAM		0.0999	99.9	-0.1	0.52
Glibesyn 5 mg	DM	1.0×10^{-4}	0.1006	100.6	0.6	0.46
	SAM		1.0032	100.3	0.32	0.23
	DM	1.0×10^{-3}	9.926	99.26	-0.74	0.82
	SAM		9.944	99.44	-0.56	0.76

Table 3. Results of commercial drug recovery and standard deviation obtained employing membrane I. (MEF - (MIP + DBPH

Pharmaceutical Drug	Potentiometric method	Prepared for concentration (M)	Concentration ($\times10^{-5}$ M)	%Rec.	%RE	%RSD
Daonil 5mg	Direct method	1×10^{-4}	10.09	100.96	0.96	0.92
	SAM		9.977	99.77	-0.23	0.43
	Direct method	1×10^{-3}	1.009	100.92	0.08	0.7
	SAM		99.8	99.8	-0.2	0.35
Glibesyn 5 mg	Direct method	1×10^{-4}	9.91	99.1	-0.9	0.9
	SAM		9.991	99.91	-0.09	0.68
	Direct method	1×10^{-3}	100.9	100.9	0.9	0.91
	SAM		99.1	99.1	-0.9	0.48

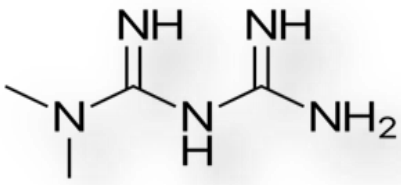
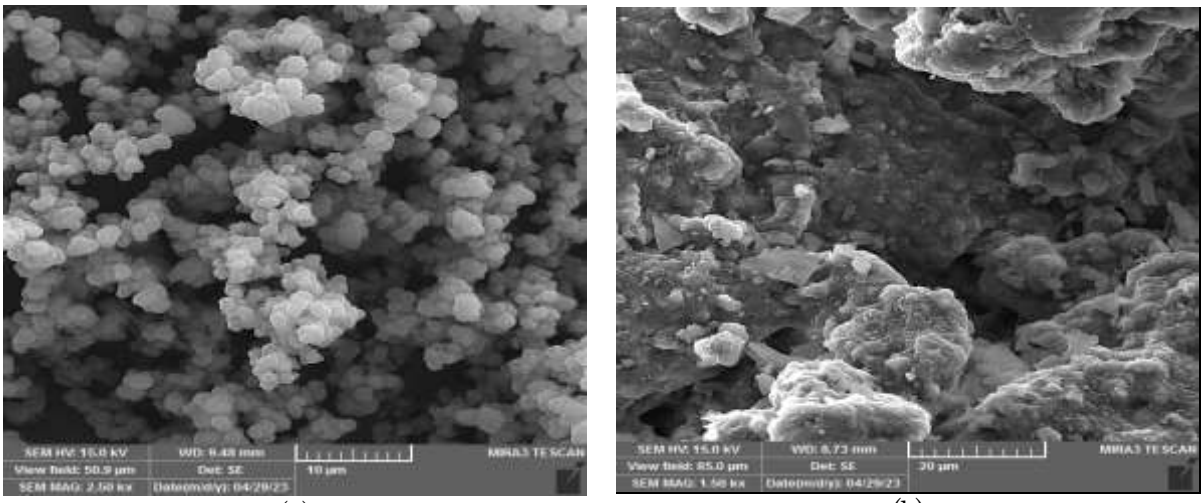


Figure 1: Structure of Metformin



(a) (b)

Figure2. The SEM images of the MIP and NIP membranes for metronidazole benzoate (A) Before removing MEF (B) After removing MEF.

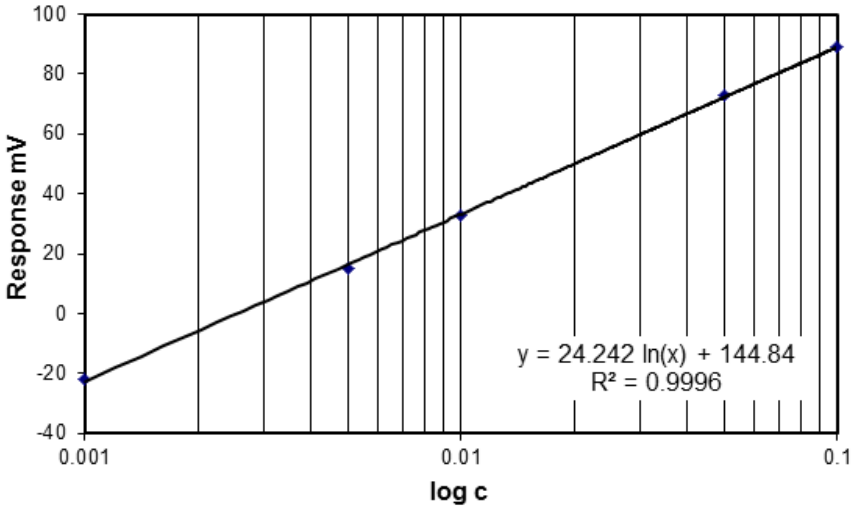


Figure3. Antilog (E/S) variation of synthetic 10^{-3} M solution compared to regular MEF applied utilizing MEF - (MIP +DOPH)

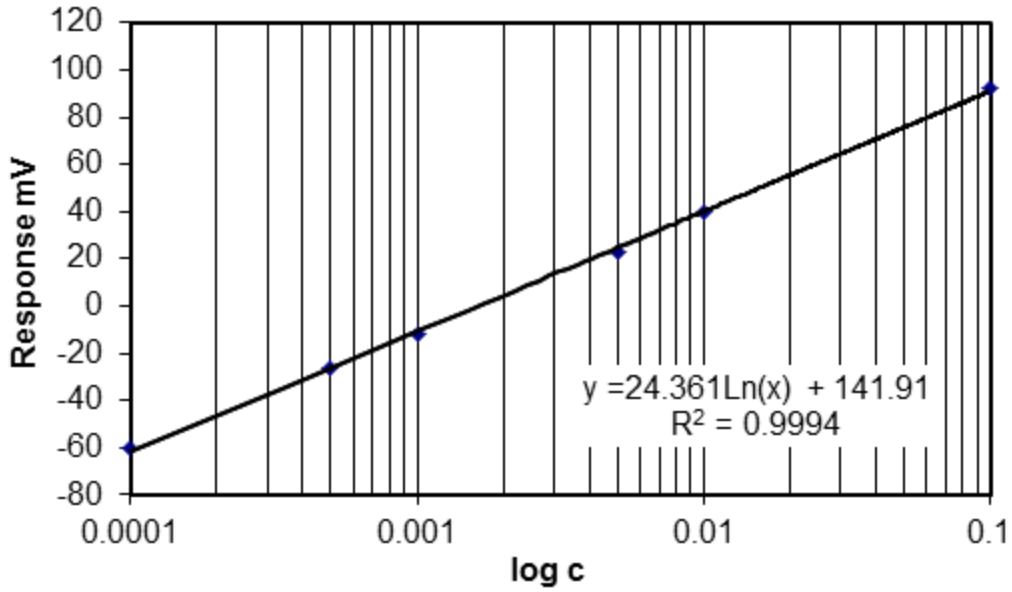


Figure4. Antilog (E/S) variation of synthetic 10-3 M solution compared to regular MEF applied utilising MEF - (MIP + DBPH)

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