ISSN: 0067-2904

Synthesis and Analysis of PVC Selective Membrane for Determination of Diazepam Based on Bulk Molecular Imprinted Polymer

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Received: 4/6/2023 Accepted: 28/12/2023 Published: 30/1/2025

Abstract

study developed two electrodes using molecularly imprinted polymers (MIP) for the selective recognition of Diazepam (DZP). Ethylene glycol dimethacrylate (EGDMA) was employed as the cross-linking monomer to polymerize allyl bromide, which acted as the functional monomer. DZP was used as the template molecule during the polymerization process to introduce recognition sites in the polymer matrix complementary to its size, shape and functional groups. For comparison, non-imprinted polymers (NIP) were also synthesized using an identical combination of EGDMA and Allyl bromide as the MIP, but without the incorporation of the DZP template. Evaluations are conducted on the slop is 29.31258 and 25.818933, linearity range (M) 5×10-5-1×10-2,5×10-5-1×10-2, correlation coefficient 0.9964,0.9994 and the detection limit (M)5.5×10-6 - 5×10-6 relatively for DIA-MIP electrodes. Selectivity tests were performed for the interfering cations Al3+, Ca2+ and K+, which showed no inhibition of diazepam detection by the proposed electrode. The generated MIP electrode exhibited promising analytical characteristics, such as good selectivity against common interfering species.

Keywords: Molecularly imprinted electrode, diazepam, potential metering, (bromide) monomer, different plasticizers (TCP) (DBP).

تحضير بوليمر جديد مطبوع جزيئيًا واستخدامه في الاستخلاص الانتقائي لتقدير دايسبام في المستحضرات الصيدلانية

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الخلاصة

طورت هذه الدراسة قطبين كهربائيين باستخدام البوليمرات المطبوعة جزيئيًا (MIP) للتعرف الانتقائي على الديازيبام (DZP). تم استخدام ثنائي ميثاكريلات جلايكول الإيثيلين (EGDMA) كرابط تشابك بروميد الأليل والذي كان بمثابة المونومر الوظيفي. تم استخدام DZP كجزيء القالب أثناء عملية البلمرة لإدخال مواقع التعرف في مصفوفة البوليمر المكملة لحجمها وشكلها ومجموعاتها الوظيفية. للمقارنة، تم أيضًا تصنيع البوليمرات غير المطبوعة (NIP) باستخدام مزيج مماثل من EGDMA وبروميد الأليل مثل MIP، ولكن بدون دمج قالب DZP. تم إجراء التقييمات على الميل 29.31258 و 25.818933، المدى الخطي (M)

*Email:Maryam.12emad@gmail.com

(وحد الكشف 0.9964,0.9994 معامل الارتباط ،5×10−5−1×10−2,5×10−5−1×10−2
6−10×5 − 6−10×5.5(M نسبيًا للأقطاب الكهربائية DIA−MIP. تم إجراء اختبارات انتقائية للكاتيونات المسببة للتداخل Al3+ وCa2+ وK+، والتي أظهرت عدم وجود تثبيط للكشف عن الديازيبام بواسطة القطب الكهربائي المقترح. أظهر القطب MIP الذي تم إنشاؤه خصائص تحليلية واعدة، مثل الانتقائية الجيدة ضد الأنواع المسببة للتداخل الشائعة.

الكلمات المفتاحية: القطب المطبوع جزيئيا، الديازيبام، قياس الجهد، مونومر (بروميد)، الملدنات المختلفة (DBP) (TCP).

1. Introduction

Diazepam (7-chloro-1,3-dihydro-1-methyl-5-phenyl-2H-1,4-benzodiazepin-2-one) is one of the most commonly prescribed benzodiazepines due to its therapeutic action as a hypnotic, tranquilizer, anticonvulsant, and muscle relaxant[1]. As the primary drug used for these indications, there is a clear need in forensic and clinical toxicology fields for rapid and accurate methods to screen biological matrices like urine and serum for the presence of diazepam and other toxins/drugs. Such analytical techniques could aid in efforts like monitoring patient compliance with prescribed treatments, investigating potential overdoses or drug-facilitated crimes. The development of quantitative and selective detection platforms for complex body fluids would benefit applications ranging from healthcare to law enforcement where screening of diazepam and associated substances is required[2]. One of the most widely prescribed 1,4-benzodiazepines is diazepam, which is also marketed under the brand name Valium[3]. consequences of sleeping pills. A benzodiazepine called DZP gives gamma-aminobutyric acid a positive allosteric regulation receptor, which increases the amount of GABA molecules that bind to the receptor. This alteration will have a relaxing impact by causing GABA receptors (channel ligand) to repolarize [4]. The central nervous system contains the receptors, which provide an explanation for how DZP causes fatigue and lowers stress levels. DZP is regarded as a drug class of psychoactive medicines in Indonesia, where government regulation governs its prescription. One must consult a doctor and receive a prescription in order to obtain DZP [5]. The new analytical approaches are based on ultraviolet-visible (UV-VIS) spectrophotometry and fluorimetry considered as the most acceptable techniques in pharmaceutical determination. Spectrophotometric techniques involve measuring the absorption spectra of diazepam in methanolic potassium hydroxide solution. Fluorimetric methods exploit the selective fluorescent properties of diazepam under alkaline conditions. Several studies have demonstrated that fluorescence detection provides high selectivity and high linearity range for diazepam with low detection limits, making it suitable for trace analysis in different matrix. For fluorimetric methods, the detection limit is 16.47 ngml-1. It has been shown that fluorimetric techniques are low detection limit and selective[6], The RP-HPLC method is the development and approval of a simple reverse phase HPLC method for measuring pills containing diazepam. The limit of detection (LOD) is 0.898 mg/ml. [7] GLS Methods for determining the amounts of diazepam (Valium) in human whole blood include gas liquid chromatography, selective ether extraction of diazepam, and acid hydrolysis. A LOD of 5.0 ng/ml is the limit of detection [8]. The method of colorimetry Benzodiazepam is hydrolyzed with 6/V HC1 to provide 2-methylamino-5-chlorobenzophenone. After extracting the chemical with chloroform, a yellow solution whose absorbance is measured at 410 nm in relation to a solvent blank is produced. Limit of detection, or LOD, is 0.1 g/ml. [9] LC-MS-MS as well. In this work, a previously established sensitive and specific LC-MS-MS detection approach was used to analyze urine, hair, and preserved oral fluid samples. This method allowed for the simultaneous measurement of tetrazepam, diazepam, nordiazepam, oxazepam, and temazepam. The 25 ng/mL limit of LOD detection [10].

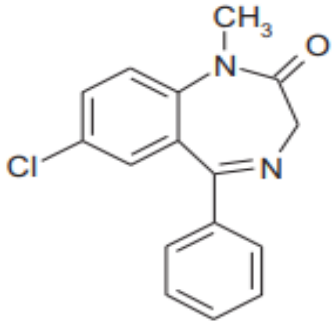

Figure 1: The chemical structure of Diazepam [11]

In this work identify the MIP preparation was performed in conjunction with the recognition cite allyl bromide with crosslinking ethylene glycol dimethacrylate EGDMA C10H14O4, whereby benzoyl peroxide BPO functioned as the target molecule (diazepam) initiator. This study aimed to evaluate both of selectivity and sensitivity of the proposed molecularly imprinted polymer (MIP) sensor for analyzing diazepam in different matrices. The effects of using different functional monomers, cross-linking agents, and solvent systems on the diazepam imprinting and adsorption behavior within the polymer matrix were also examined. Scanning electron microscopy was used to analyze the surface morphology of the MIP, while Fourier transform infrared spectroscopy was employed to characterize the functional group interactions involved in the imprinting process.

2. Experimental

2.1. Materials and chemicals

Diazepam reference standard was obtained from the Iraqi State Corporation for Pharmaceutical and Medical Equipment Industries (IRAQ - SID - Samara). Additionally, commercial diazepam-containing formulations including VALIAPAM 10 tablets (500 mg diazepam per tablet) manufactured by SDI-Iraq and Valium 10 tablets (5 mg diazepam per tablet) produced by an Australian pharmaceutical company were purchased from local pharmacies. Plasticizers were obtained from Sigma-Aldrich; dibutyl phthalate (purity of 97.0%) and tricresyl phosphate (90%) were used as received. Allyl bromide was utilized as a monomer; Sigma-Aldrich provided the ethylene glycol di methacrylate (EGDMA) and 78% of the benzoyl peroxide (BPO). The chemicals utilized were of the purest concentration of reagents and were used without purification.

2.2. Preparation of MIP and NIP

For the synthesis of the diazepam molecularly imprinted polymer (DZP-MIP1), 1 mg of diazepam (0.131 g) was dissolved in 1 mL of functional monomer allyl bromide. To this solution, 0.3 g of initiator benzoyl peroxide was added, followed by the addition of 3.77 mL of cross-linker ethylene glycol dimethacrylate (EGDMA). The mixture was agitated for 5 minutes to form a homogeneous polymeric precursor solution. Nitrogen gas was bubbled through the solution for 20 minutes to remove any dissolved oxygen, thereby facilitating polymerization upon initiation. The nitrogen purging ensured an oxygen-free environment suitable for radical polymerization triggered by the initiator. This process yielded a diazepam-imprinted polymeric matrix bearing recognition sites complementary to the target analyte. After that, the tube was put in. a water bottle that is 65 degrees Celsius. As soon as the process was finished, the molecularly imprinted polymer totally hardened and broke down into a microscopic polymer particle after the polymerization process. This substance was

subjected to sonication. in a 9:1 mixture of CH3OH and CH3COOH, eliminating the MIP sample document. How big are dia-MIP1 particles (75-125 m)The same materials and processes can be used to create non-molecularly imprinted polymers as for molecularly imprinted polymers. DZP - MIP1, but without the template (diazepam)[12 ,13].

2.3. Instruments

This study used a WTW model ion analyzer, a WTW model pH 720 pH meter, and a saturated calomel electrode (Gallenkamp, USA). The diazepam-MIP was fabricated as an electrode in a test tube, and all potentiometric experiments were conducted at room temperature. Along with the Ag-AgCl reference electrode, the diazepam-MIP working electrode contained a 0.1 M diazepam solution as the internal filling solution. Placing the PVC tube (1-4 cm in length) in a clear dish and soaking it in THF caused it to become flattened and polished. A membrane was trimmed to match the outer diameter of the PVC tubing and adhered to the precise result. The opposite orientation of the PVC and, finally, the tubing was fastened towards the electrode device. The electrodes were optimized by thoroughly soaking them in a 0.1 M diazepam solution for at least three hours before use.

2.4. The preparation of standard solutions

A standard 0.01 M diazepam solution was prepared by dissolving 0.1423 g of pharmaceutical-grade diazepam in methanol. The solution was then diluted to 50 mL in a volumetric flask with methanol as the solvent. Using the direct method, the additional solutions were produced in 50 mL at concentrations ranging from ($5x10^{-5}$ to 10^{-2}) M. all interferences cations (Al^{3+}, Ca^{2+}, and K^{+}) were made as a 0.1 M stock solution at concentrations ranging from ($5x10^{-5}$ to 10^{-2}) M and then prepared of 100 mL

2.5. Synthesis of Membrane Molecularly Imprinted Polymers Electrode

Based on the methods of Thomas and Moody[14, 15], the diazepam membrane was immobilized within a PVC tube. 0.036g of DZP-MIP was combined with 0.45g of plasticizers used in this study, including TCP for electrode M1 and DBP for electrode M2. 0.2g of PVC powder was added as a supporting structure for the membrane. The materials were mixed with 7 mL of tetrahydrofuran until a thick, viscous liquid was obtained. The mixture was stirred continuously until fully combined and homogeneous. The liquid was then poured into a glass ring measuring 30-35 mm in diameter placed on a flat glass slide topped with a filter membrane. The solvent was allowed to evaporate at room temperature for 24-48 hours to form the membrane. The obtained membrane had a varied thickness than other membranes, ranging between (0.4) and (0.7) mm. This membrane size was appropriate for preparing electrodes.

2.6. Construction of Ion-Selective Electrodes

The construction and immobilization of the electrode were achieved as described by Mahajan et al. [16]. An internal fluid of 0.1 M diazepam had been added to the glass tube. The membrane electrode needs to be soaked for at least two to three hours before actual metrics in a standard (0.1) M diazepam solution.

2.7. Preparation of Pharmaceutical Samples

The tablet samples were crushed using a mortar and pestle in order to extract the active components from the pharmaceutical formulations. 0.4g of the crushed sample was weighed out in advance to be used in preparing a 50 mL solution. Pharmaceutical samples were dissolved using the 99% methanol concentration (CH3OH), and the volumetric flask was filled to the brim with methanol and stirred for over half an hour. The fluid was filtered

through 0.07 m cellulose filter paper to get 5 x 10-3 M and 5 x 10-4 M diazepam concentrations.

3. Results and Discussion

The diazepam MIP was characterized by first using UV-Vis spectroscopy to identify the drug's absorption wavelength. As demonstrated in the figures, a preliminary diagnosis was made to confirm the presence of the drug in this imprint.

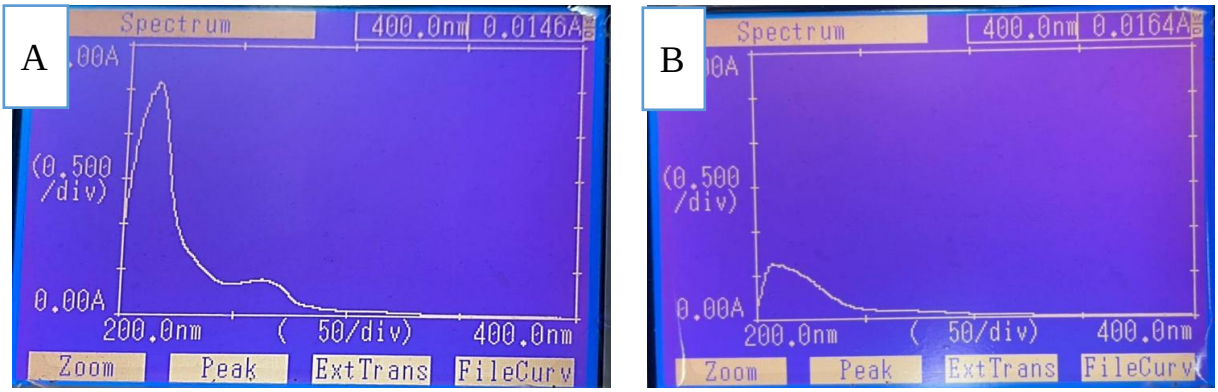

Figure 2: A and B the absorption of diazepam drug at 262 nm before and after extraction

3.1 FT-IR analysis

Molecular imprinted polymer was synthesized using bulk polymerization (non-covalent). A functional monomer played a crucial role in researching interactions with the template. The MIP and NIP were made using ethylene glycol di methacrylate as the monomer. FTIR analysis is an essential chemical characterization technique for detecting functional groups in a molecule. The FTIR spectra of various MIP and NIP are presented in Table (1), Figures 3,4

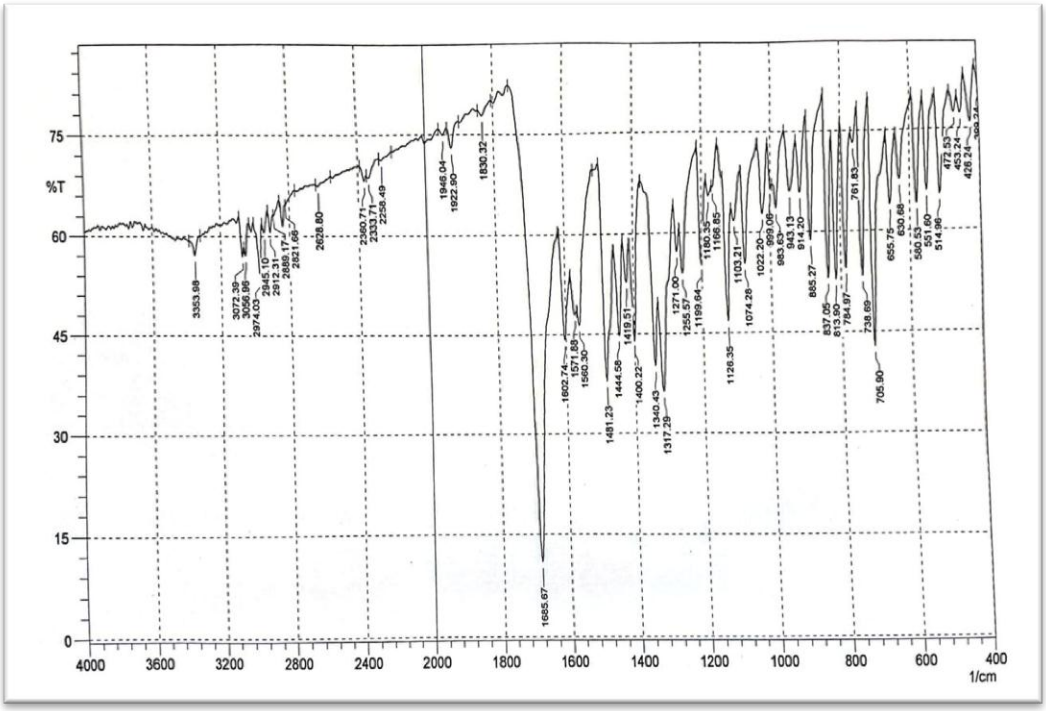

Figure 3: FTIR spectra of diazepam standard.

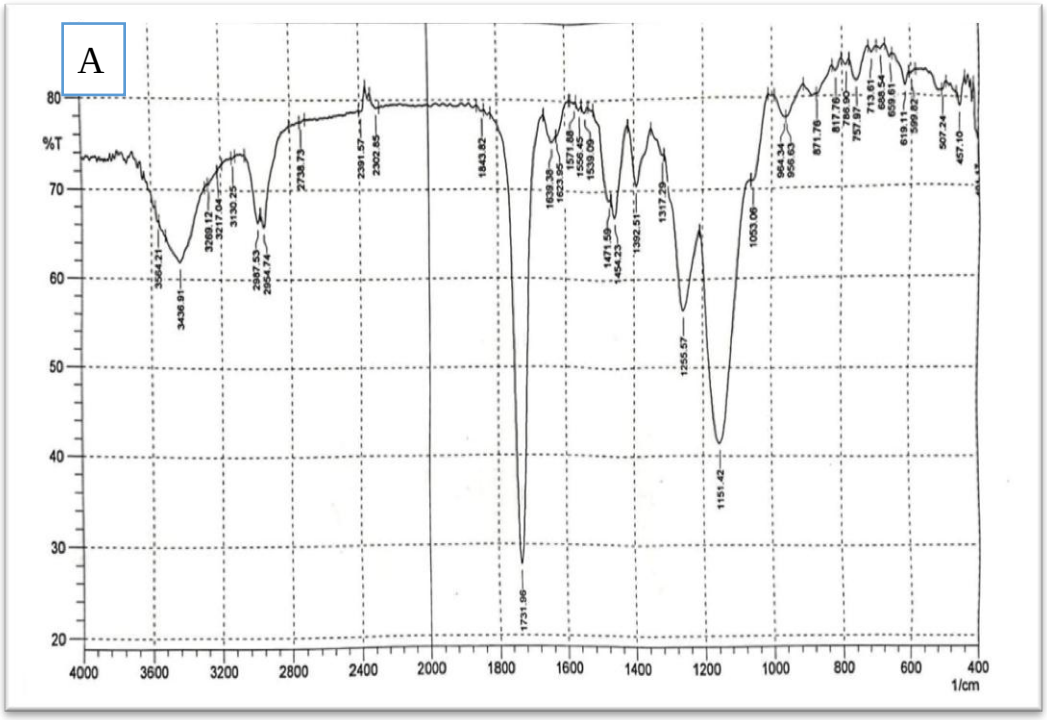

Figure 4A- FTIR spectrum of DZP-MIP (after removal of the template (diazepam).

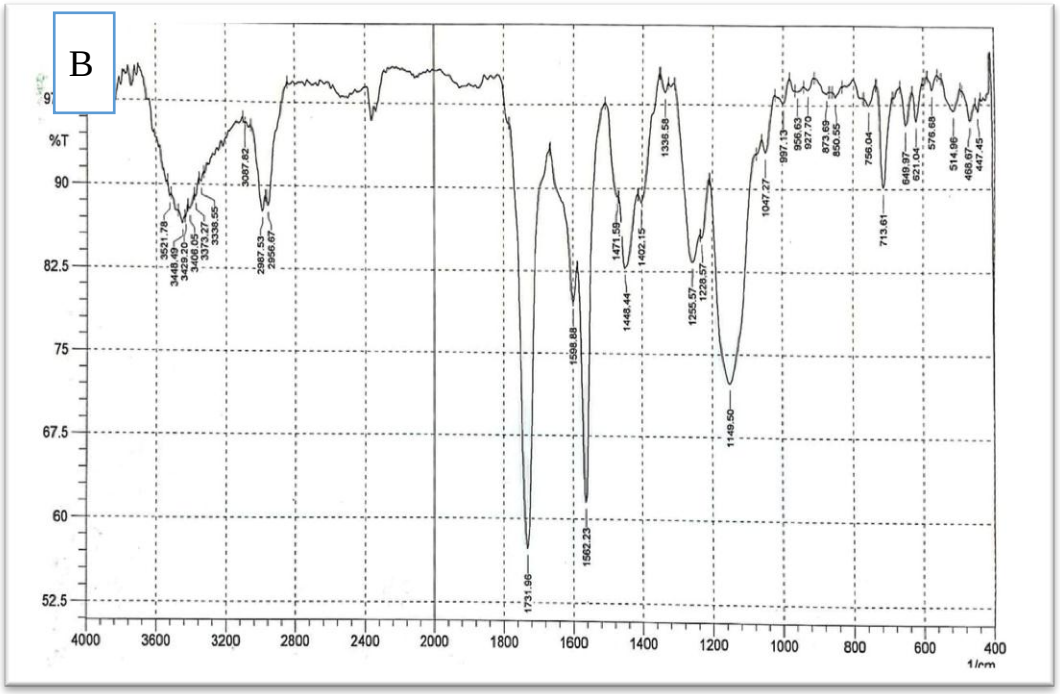

Figure 4B- DZP-MIP's FTIR spectrum before and after elimination (before the template (diazepam) is removed).

Table 1: The bands and the structures of the primary three DZP-MIP compositions show MIP both before and after the removal template**.**

Template (Diazepam)	Monomer (Allyl bromide)	Cross linker (Ethylene glycol di methacrylate)	
Band	**Drug(Template)**	**MIP before extraction**	**MIP after extraction**
N C-H $_{\text{aliph. str.}}$	2965,2934	2973,2952	2976,2935
N C-H $_{\text{aromatic str.}}$	3065	3173	-
N O=C-N $_{\text{str. amid}}$	1658	1643	-
N C=C $_{\text{aromatic. str.}}$	1610	1535	-
N C-Cl	878	876	873
N N-C=O $_{\text{carbonyl str.}}$	--	1728	1730

The Fourier transform infrared spectroscopy (FTIR) spectra of the leached and released diazepam (DZP) imprinted polymer (MIP) and non-imprinted polymer (NIP) were recorded using the KBr pellet method over the range of 400-4000 cm-1 (Table 1). The FTIR spectrum of atemozolomide showed bands corresponding to: aromatic C-H stretching, aliphatic C-H stretching, N=O-C-N stretching amid, and aromatic C=C stretching (2945, 2912, 3056,1685, 1602, and 813) cm-1. Additional bands were observed for carbonyl C=O and N-C-Cl stretching. The diazepam MIP FTIR spectrum prior to template removal showed bands for aromatic C-H stretching, aromatic N=O-C-N stretching, and aromatic C=C stretching at 3180, 1639, and 1554 cm-1 respectively. The drug has been removed from the template, as evidenced by the lack of N C-H aromatic stretching, NO=C-N aromatic stretching, and N C=C aromatic stretching in the MIP(DZP) FTIR spectrum after template removal. The FTIR spectra of the MIPs before and after removing the template and NIP are displayed in Table 1 for the other MIPs for Diazepam (DZP) that were created using allyl bromide as a monomer [17].

The linear range, correlation coefficients, detection limits, and lifespan in days of the DZP-MIP membrane-based electrodes were evaluated. Table 1 and Figures 4A and 4B present the results of these assessments, consistent with previous reports.

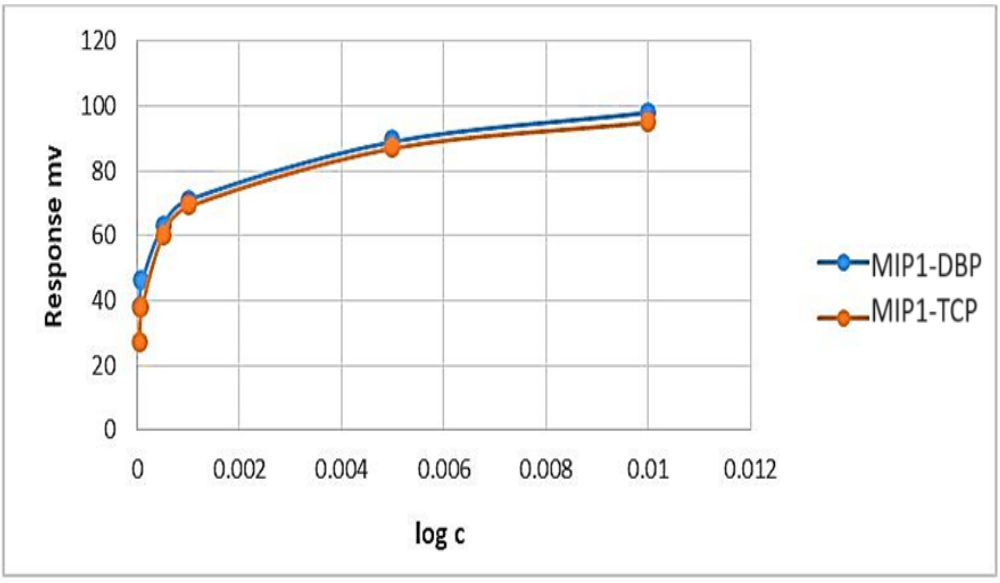

Figure 6: Calibration curve for DZP-MIP membrane electrodes

Table 2: Features of the diazepam-MIP electrode composed of many useful monomers and plasticizers

Membrane composition	DZP-MIP+TCP(M1)	DZP-MIP+DBP (M2)
Slop (mV/decade)	28.81	**29.98**
Linearity range (M)	5×10^{-5}-1×10^{-2}	**5×10^{-5}-1×10^{-2}**
Correlation coefficient	0.9995	**0.9946**
The detection limit (M)	5.2×10^{-6}	**5.8×10^{-6}**
Lifetime (day)	15	**11**

3.2. Effect of pH on electrodes response

Using allyl bromide as a precursor and diazepam as a template, two electrodes were created. On DZP membrane electrodes with different DZP concentrations (5×10-3 and 5×10-4), a pH study was carried out. pH testing (1–11) in pH research uses NH4OH (0.1M, 1M) or HCl acid (0.1M, 1M). The final results obtained by including the appropriate amount of HCl/NH4OH are as follows, as shown in Table (3) and Figure 7. The variation in pH-value related potential is caused by the electrode composition [18].

Table 3: Working pH range for Selective diazepam electrode

Number and design of MIPs	Membranes	Membrane design	pH range	
			5×10^{-3}	**5×10^{-4}**
MIP DZP+EGDMA+ALL	M1	DZP-MIP+TCP	5.6-8.7	5-9
	M2	DZP-MIP+DBP	3-2.5.4	4.6-7.9

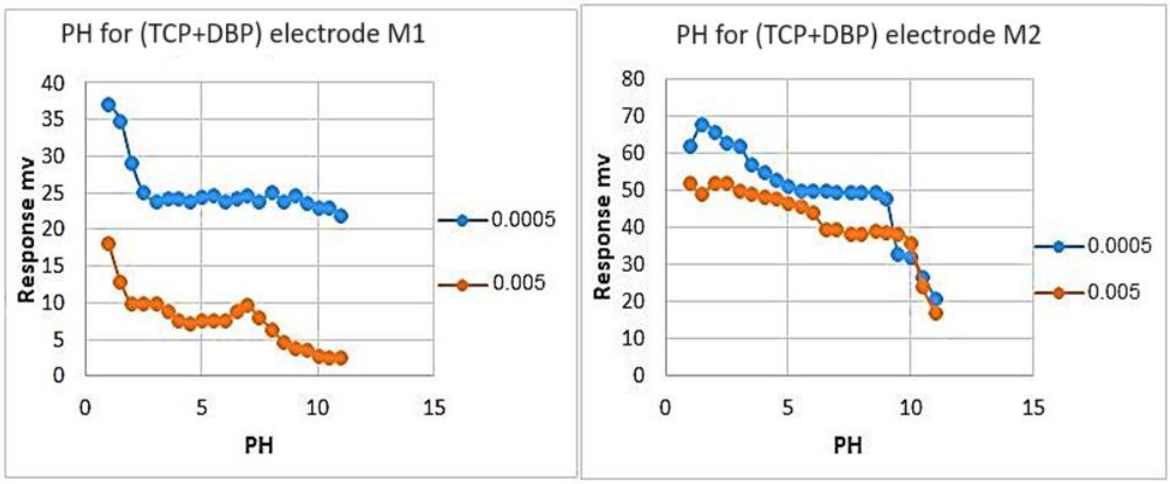

Figure 7: Effect of pH on the diazepam electrodes at 5×10-3 and 5×10-4 concentrations (A(DZP-MIP + TCP(M1)) and B(DZP-MIP + DBP (M2)).

Interference studies

Two electrodes were fabricated using allyl bromide as a precursor and diazepam as the template molecule. To calculate the selectivity coefficients of the electrodes, a separate solution method was employed using potassium chloride as the primary ion instead of the standard mixed solution method. Apply the special formula needed for these parameters, which is represented by the equation that follows[15] :

$$\text{Log K pot} = [(EB - EA)/(2.303RT/z\,F)] + (1 - zA/zB)\log aA \quad (1)$$

Where EA, EB, zA, zB, and aA are, in order as well as the charges, potentials, and actions of when aA = aB, the main A ions and the interfering B ions.

The results of this inquiry include the primary ion selectivity coefficients and interference from additional ions like (K^+, $Ca^{2+,}$ and Al^{3+}. The selectivity coefficients are affected by the

concentration and make-up of the electrodes, the primary and secondary ion interference charges, and other factors. The ions that interfere with the drug were taken, and the interfering substances will be studied in the future and compared with the doses present in the drug .The selectivity coefficient values were displayed in Figures 8 and 9 and Tables 4 and 5. Using several DZP membrane electrodes.

Table 4: Selectivity coefficients for (DZP-MIP+TTP) electrode at different concentrations of diazepam.

Conc.	Concentrations of Diazepam (M): concentrations of interference ions (M)					
	Interfering ions					
	Al^{3+}		Ca^{2+}		K^{+}	
	E_B (mv)	$K_{A,B}$	E_B (mv)	$K_{A,B}$	E_B (mv)	$K_{A,B}$
10^{-2}	45	1.6563×10^{-2}	41	2.3870×10^{-3}	34	5.7847×10^{-4}
5×10^{-3}	43	2.8562×10^{-2}	35	1.1647×10^{-3}	27	1.6327×10^{-4}
1×10^{-3}	40	9.8368×10^{-2}	32	8.9287×10^{-4}	24	1.0213×10^{-4}
5×10^{-4}	33	9.8568×10^{-2}	28	3.0876×10^{-4}	19	3.8651×10^{-5}
5×10^{-4}	22	3.1354×10^{-1}	23	3.4654×10^{-4}	16	2.9620×10^{-5}
5×10^{-5}	21	2.6464×10^{-1}	17	2.1765×10^{-4}	12	1.1787×10^{-5}

Table 5: Selectivity coefficients for the electrode (DZP-MIP+DBP) at various diazepam concentrations.

Con.	Concentrations of Diazepam (M): concentrations of interference ions (M)					
	Interfering ions					
	Al^{3+}		Ca^{2+}		K^{+1}	
	E_B (mv)	$K_{A,B}$	E_B (mv)	$K_{A,B}$	E_B (mv)	$K_{A,B}$
10^{-2}	43	2.6540E-02	43	4.7341E-03	38	1.9647E-03
5×10^{-3}	42	3.6742E-02	38	1.8327E-03	35	5.7297E-04
1×10^{-3}	41	1.0769E-01	36	1.5342E-03	29	3.6984E-04
5×10^{-4}	31	1.4982E-01	28	5.0769E-04	24	1.0831E-04
1×10^{-4}	29	7.3626E-01	15	2.9920E-04	22	6.5187E-05
5×10^{-5}	24	2.8872E-05	11	1.5762 E-05	19	1.5342E-05

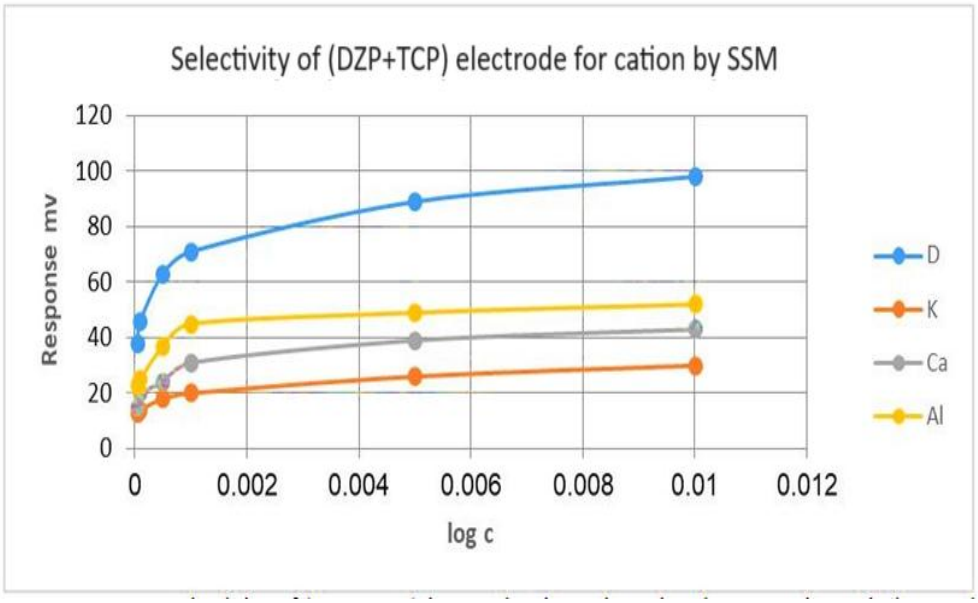

Figure 8: Selectivity of the separation solution method for (DZP+TCP) ions at the electrodes

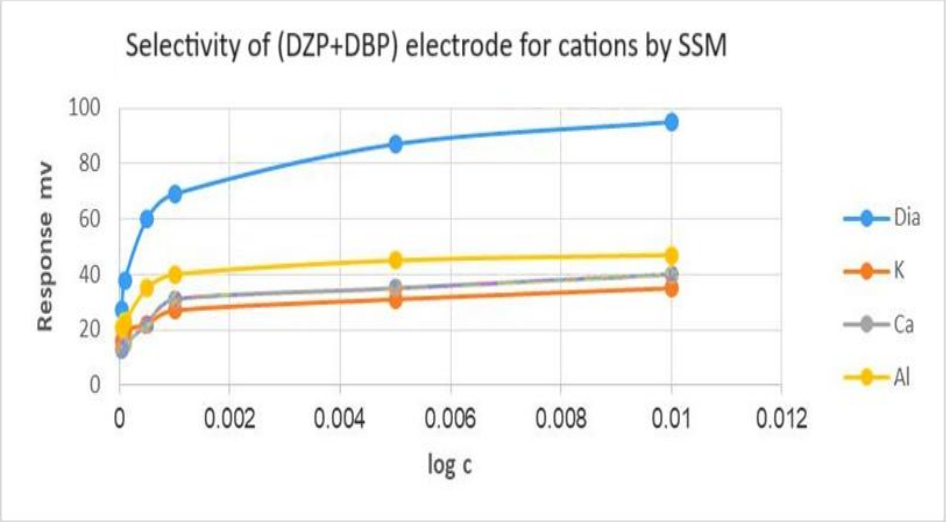

Figure 9: Selectivity of the separation solution method used to (DZP-DBP) ions at the electrodes

3.4. Calculation by multiple standard addition method (MSA*)*

Linear regression calibration plots of the antilogarithm of sensitivity (E/S, y-axis) versus standard concentrations of diazepam (x-axis) were constructed at 5x10-3 and 5x10-4 mol/L. The findings of our diazepam ratio computations based on electrodes on DZP-MIP+ TCP and DZP-MIP+DBP are shown in Figures (10, 11). These computations were carried out on electrodes of DZP membrane using different DZP concentrations.

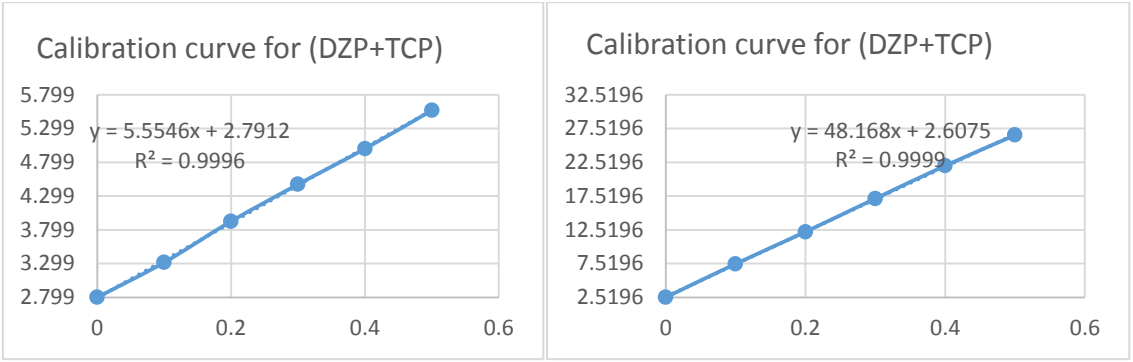

Figure 10: Antilog (E / S) in relation to the entire volume of the elevated standard in order to use (DZP–MIP + TCP) electrode to determine diazepam solution (A 5×10-3 and B 5×10-4) by MSA.

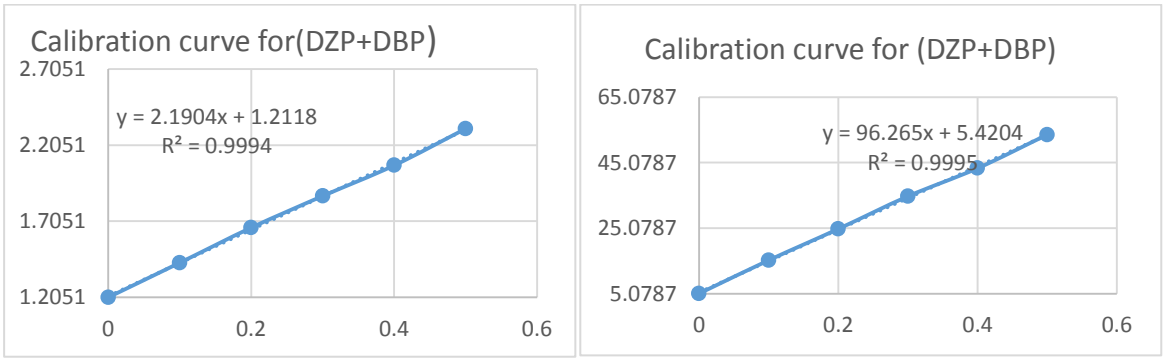

Figure 11: Antilog (E / S) in relation to the increased standard's total volume in order to use

the (DZP–MIP+ DBP) electrode to determine the diazepam solution (A 5×10-3 and B 5×10-4) through MSA.

3.4. Applications of pharmaceuticals.

MIP-based ion selective electrodes were utilized to determine diazepam in medicines. This ISE includes standard addition, direct, Gran plot, and multiple standard addition measurements. They were two concentrations of Diazepam (5x10-3and 5x10-4) M taken for application to commercial drugs. The RE%, RC%, and RSD% of Diazepam in medicinal use were calculated, shown in Table (6).

Table 6: Diazepam samples are determined using PVC membrane-based ion selective electrodes (ISEs) procedures.

Electrode No.	Concentration (M)			
	Sample	Measurement using potentiometric methods		
		Direct	SAM	MSA
DZP-MIP+TCP	5×10^{-3}	5.0145×10^{-3}	5.0165×10^{-3}	5.0102×10^{-3}
	RSD%	1.45	1.62	…….
	RC%	100.29	100.33	100.204
	RE%	0.29	0.33	0.204
	5×10^{-4}	4.911×10^{-4}	5.0534×10^{-4}	4.9977×10^{-4}
	RSD%	1.28	1.91	…….
	RC%	98.28	101.25	99.95
	RE%	-1.78	1.56	-0.05
Electrode No.	Concentration (M)			
	Sample	Measurement using potentiometric methods		
		Direct	SAM	MSA
DZP-MIP+DBP	5×10^{-3}	5.0332×10^{-3}	5.0261×10^{-3}	4.98×10^{-3}
	RSD%	1.52	1.74	……
	RC%	100.664	100.522	99.6
	RE%	0.664	0.522	-0.40
	5×10^{-4}	5.0178×10^{-4}	5.0618×10^{-4}	4.9848×10^{-4}
	RSD%	1.5744	0.51	……..
	RC%	100.36	101.236	99.7
	RE%	0.36	1.236	-0.3

Table 6 shows that the first electrode, MIP1-TCP, is the most accurate when comparing the results in the three-methods for two electrodes. This is because of its plasticizer viscosity, which is TCP = 26 and DBP = 9 Mpa.s.

Table7: Sample analyses of pharmaceutical Diazepam using DZP-MIP+TCP electrode.

pharmaceutical	(Iraq)		
Concentration prepared	Direct	SAM	MSA
	5×10^{-3}	5×10^{-3}	5×10^{-3}
found	4.9277×10^{-3}	4.9929×10^{-3}	4.9304×10^{-3}
RC%	98.55	99.85	98.61
RSD%	1.4089	1.02	……..
RE%	-1.45	-0.14	-1.39
F experimental	6.3	4.8	2.7
F theoretical	19.2		
pharmaceutical	Direct method	SAM	MAS
Concentration prepared	5×10^{-4}	5×10^{-4}	5×10^{-4}
Found	4.8468×10^{-4}	5.0499×10^{-4}	4.9792×10^{-4}
RSD%	2.232	0.77	……..
RC%	98.69	100.998	99.58
RE%	-1.31	0.998	-0.42
F experimental	3.9	2.1	1.6
F theoretical	19.2		

Table 8: Sample analyses of pharmaceutical diazepam using DZP-MIP+DBP electrode.

pharmaceutical	(Iraq)		
Concentration prepared	Direct	SAM	MSA
	5×10^{-3}	5×10^{-3}	5×10^{-3}
found	4.9642×10^{-3}	4.9729×10^{-3}	4.9622×10^{-3}
RC%	99.29	99.458	99.24
RSD%	0.7683	1.02	…….
RE%	-0.71	-0.542	-0.76
F experimental	7.1	4.8	2.4
F theoretical	19.2		
pharmaceutical	Direct method	SAM	MAS
Concentration prepared	5×10^{-4}	5×10^{-4}	5×10^{-4}
Found	4.9524×10^{-4}	5.01×10^{-4}	4.9838×10^{-4}
RSD%	1.1788	0.5086	……..
RC%	99.05	100.2	99.32
RE%	-0.95	0.2	-0.68
F experimental	6.3	3.1	1.4
F theoretical	19.2		

*** Each measurement was carried three times**

Conclusion

A novel molecularly imprinted polymer (MIP) was synthesized using allyl bromide as the functional monomer and ethylene glycol dimethyl acrylate as the cross-linker, with diazepam employed as the template molecule. This generated a bulk DZP-MIP material with binding sites tailored for the target analyte. To fabricate selective sensing electrodes, diazepam-imprinted polymer membranes were combined with different plasticizers including tricresyl phosphate and dibutyl phthalate to yield plasticized PVC-based membrane electrodes. Several analytical methods were conducted to make selective molecular imprinted polymers. This was performed by preparing and optimizing the needed monomers, cross-linking with the right solvents, using porogenic solvents, to remove the template, and sticking to the best molar ratios of tamplate (diazepam) to monomer for cross-linking. The results obtained for all electrodes applied to standard and medicinal solutions were excellent. The purpose of developing electrodes for use in pharmaceutical analytical determination.

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