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DETERMINATION OF CEFALAXIN IN PHARMACEUTICAL PREPARATION BYMOLECULARY IMPRENTED POLYMER IN PVC MATRIX MEMBRANE

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ABSTRACT

This current study was built on creating four electrodes based on molecularly imprinted polymers (MIPs). As the template using Cefalexin (CFX), 1-vinyl imidazole (VIZ) and vinyl acetate (VA) as monomer, and N, N-methylene bis acrylamide (MBAA) as cross-linkers and benzoyl peroxide as the initiator, two MIPs were prepared. The same composition was used in non-impressed polymers (NIPs) preparation, but without the template (Cefalexin). For the membranes preparation, numerous plasticizers, such as tri-oly phosphate (TOP) and di-octyl phthalate (DOP), were used in the PVC matrix, slop, detection limit, lifetime, and linearity range of CFX-MIPs electrodes are characteristics studied. To describe the created MIP, scanning electron microscopy (SEM) was used to study the properties of the electrodes, the slope, the detection limit, and the life time and linearity range. The effect of PH and interference on the efficiency of the electrode MIP was also investigated. The study has shown that the molecularly imprinted electrodes have high sensitivity and responsiveness to cefalaxin. The DPV value was linearly dependence on the aspirin concentration and a linear curve was obtained within the range of (1×10−1 - 5×10-4) M of cefalaxin with correlation coefficients are about (0.9941, 0.9899, 0.9936 and 0.9837) with slops value of (-18.48, -18.84, -18.60 and -19.47) and the detection limit for all electrodes ranging from (6×10-1-9×10-1) M.In the selectivity measurements results that we obtained there's no interaction with the cefalexin drug on interfering cations (K+, Ca+2, Al+3) and certain pharmaceutical additives such as methylparaben, propylparaben and trisodium citrate. The preparation electrodes have been shown good response including testing pharmaceutical analysis.The strategy employed is easy and fast. CFX membranes also have a short reaction speed, excellent mechanical stability, are removable and quick to create.

Keywords: Molecularly imprinted polymers(MIP), Cefalexin , vinyl acetate (VA) monomer, 1-vinylimidizol (VIZ) monomer.

المجلة العراقية لبحوث السوق وحماية المستهلك
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تقدير عقار السيفالكسين في المستحضرات الصيدلانية باستخدام الطبعة الجزيئية البوليمرية في قالب متعدد كلوريد الفينايل

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الخلاصة

لتقدير السيفالكسين، تم إنشاء أقطاب بوليمرية مطبوعة جزيئيا MIP-CFX عن طريق البلمرة الالكترونية، تم تحضير الأقطاب الكهربائية عن طريق الجمع بين القالب (السيفالكسين) مع (الفينيلأسيتات (VA)، ١-فينيل ايميدزول (VIZ)) كمونومروظيفي و N و N- ميثيلين بيساكريلاميد (MBAA) كموصلات متشابكة وباستخدام البنزويل بيروكسايد (BPO) كبادئ، تم تحليل كفاءة الأقطاب الكهربائية الغشائية بواسطة قياس الجهد التفاضلي (DPV)، تم تصنيع أربعة أقطاب كهربائية باستخدام ملدنين مختلفين وهما ثلاثي- اولي فوسفيت (TOP)، وثنائي أوكتيلفثاليت (DOP) في مصفوفة PVC. تم استخدام الفحص المجهري الإلكتروني (SEM) لوصف MIP المتولد، ودراسة خصائص الأقطاب الكهربائية، والميل، وحد الكشف، وعمر القطب، والمدى الخطي. تم فحص تأثيردرجة الحموضة وتأثير التداخلات على كفاءة القطب MIP. وقد أظهرت الدراسة أن الأقطاب التي تم طبعها جزيئيًا لها حساسية عالية واستجابة للسيفالكسين. وكانت قيم الـ DPV هي خطية اعتماد على تركيز السيفالكسين وتم الحصول على منحنى خطي ضمن حدود M (1×10^{-1}-5×10^{-4})مولاري من السيفالكسين مع معاملات الارتباط حوالي (٠.٩٨٣٧، ٠.٩٩٣٦، ٠.٩٨٩٩ و ٠.٩٤١) بقيمة انحدار تبلغ (-١٨.٨٤، -١٨.٤٨، -١٩.٦٠ و -١٤.٦٧) وحد الكشف لجميع الأقطاب الكهربائية يتراوح من (6×10^{-1}-9×10^{-1})مولاري. وقد أظهرت الاقطاب المطبوعة جزيئيًا استجابة جيدة مع قابلية عالية للتكرار وليس هناك تأثيرللتداخلات المتوفرة بشكل متكرر في المستحضرات الصيدلانية. ان النهج المستخدم سهل وسريع. كما حصلت أغشية CFX على وقت استجابة محدود، واستقرار ميكانيكي ممتاز، وقابلة للإزالة وسهلة التركيب.

الكلمات المفتاحية: الطبعة البوليمرية الجزيئية (MIP)، السيفالكسين (CFX)، مونومرأسيتاتالفينيل (VA)، مونومر ١- فينيل ايميدزول(VIZ).

INTRODUCTION

Cefalexin (CFX), regarded as the first-generation cephalosporin antibiotic shows in (Figure1) with the advantages are low cost, high inhibitory activity against a gram-positive broad spectrum and gram-negative organisms **(Nazari *et al*., 2015; Liu *et al*., 2018; Ahmed & Theydon 2012)**.It was usually functional in bovine mastitis treatment, respiratory, urinary tract infections, and other related diseases in veterinary medicine. Unluckily, the CFX misuse in livestock industry leads to residues in animal products that can enter the human body and cause many untoward effects such as indigestion, diarrhea, anorexia, nausea and vomiting **(Lata *et al*., 2015)**.

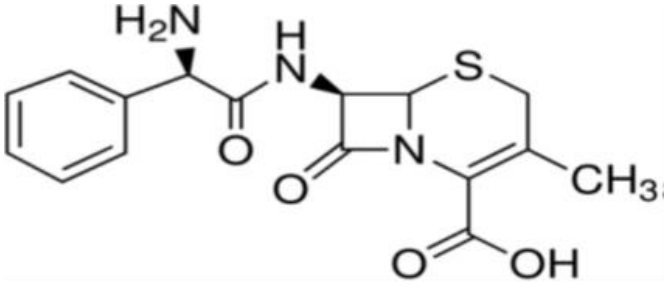

Figure (1): **Structure of Cefalexin.**

In modern years, cefalexin quantification various methods and other cephalosporins have been developed, these methods be able to subdivide into different categories: microbiological, chromatographic, spectrophotometric, and electrochemical methods.

Microbiological assay systems **(Nagel *et al*., 2012)**. Have been engaged for the cephalosporins detection in milk, but presented as main disadvantages selectivity lack and necessary for bacterial cell cultures.Also instrumental techniques have been used for cephalosporins quantification in different matrixes. These techniques include chromatographic methods such as high performance liquid chromatography (HPLC) with ultraviolet detection (UV) **(Oliveira *et al*., 2007)**. HPLC coupled with mass spectrometry (MS/MS) **(Baeza *et al*., 2016; Li *et al*., 2016)**. Si molecularly imprinted solid phase extraction (SPE) with HPLC **(Lata *et al*., 2015)**, and UV spectrophotometry **(Baeza *et al*., 2016)**.

Appropriately, all the aforementioned chromatographic techniques require difficult work protocols, qualified staff and harmful reagents use in large quantities. The spectrophotometric method needs a previous derivatization sample with 1, 2-naftoquinone-4-sulphonic **(Nishide & Tsuchida 2006)** in 1970, was first one who informed about molecular imprinting technique, Molecular imprinting is a commonly initial method to make the polymers with different Molecular properties for a given drug, its analogs, or an enantiomer **(Yan & Row 2006)**. Molecularly imprinted polymers (MIPs) are prepared by combining a template molecule with functional monomers, a cross-linker and initiator in appropriate solvent, most of the time polar and un-polar solvent after polymerization and the extraction.

Template molecule show up recognition cavities that complement form, size and template molecule chemical functionality what allowing the resulting polymers to selectively rebind template molecule from closely related compounds mix **(Lavignac *et al*., 2004;Vlatakis *et al*., 1993)**. In this analysis cefalexin was used as a template and select functional monomer of vinyl imidazole and N, N-methylene bis acrylamide (MBAA) as cross linker for the preparation MIPs. Interactions between template and monomer have been calculated through spectral and computer simulation research.

Many techniques used to define drugs and pharmaceuticals, the selective electrodes technique one of these that used for determination cefalexin because it 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 offered used for drugs analysis and ionic species **(Singh & Gupta 2006; Zamani *et al*., 2008; Ganjali *et al*., 2009)**.

Molecularly imprinted polymers (MIPs) were used the cefalexin as a template. On the opposite, the monomer was used in Vinyl acetate (VA) in addition to 1-vinyl imidazole (VIZ) and (N, N-methylene bis acrylamide (MBAA) as cross-linkers, respectively and benzoyl peroxide as an initiator to polymerization process achievement. There are a different ion-selective electrode determined drugs that depended on MIPS as recognition membranes such as diclofenac sodium, **(Al-Bayati & Abd 2017)**. Warfarin, **(Al-Bayati & Al-Safi 2018)**. Phenytoin, **(Al-Bayati & Aljabari 2016)**. And metronidazole benzoate **(Al-Bayati & Al-Safi 2018)**. This study used various plasticizers to membranes electrodes construction based on CFX-MIPS, like Tri-oly phosphate (TOP), and di-octyl phthalate (DOP).

MATERIALS AND METHODS

Preparation of MIP and NIP

To prepper first cefalexin molecularly imprinted polymer (CFX-MIP_3), bring 0.5 mmol (0.1827 g) from cefalexin then mixed with 3 mmol (0.229 g) 1-vinyl imidazole (VIZ) as monomer, after that added to solution 15 mmol (2.312 g) N, N-methylene bis acrylamide (MBAA) as the cross-linker, followed by (0.32 g) benzoyl peroxide as initiator. All these materials were dissolved in 5±mL methanol (CH_3OH) except initiator have dissolved in 3 ml chloroform. While to achieved the second cefalexin molecularly imprinted polymer (CFX-MIP6) mix 0.5 mmol (0.1827 g) from cefalexin as template, to 3 mmol (0.258 g) Vinyl acetate

(VA) as monomer, add 15 mmol (2.313 g) N,N-methylene bis acrylamide (MBAA) as cross-linker and (0.3 g) benzoyl peroxide as initiator which dissolved in 5±mL of methanol (CH_3OH). To obtain a homogeneous solution stirred the mixture for 5 minutes. N2 passes for 30 min on mixture to remove oxygen from the solution, later on put solution in a water bath, when reaction is completes 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 methanol/ CH3COOH (18:2 v/v) to remove the template from MIP. The polymer was dried for (67) hr for MIP3 and (61) hr for MIP6 at room temperature, the polymers crushed and ground by morter and sieve 125 µm particle size (using 125µm mesh sieve); after dried completely at room temp, that was used as an active substance in the selective sensors membrane. The CFX-MIP3 and CFX-MIP6 particle size were between (43-60) µm and (75-125) µm, respectively. Using the same substances and conditions that formed CFX-MIP3 and CFX-MIP6 but without the cefalxin (template) for non-molecularly imprinted polymers preparation and the same composition was used in the non-imprinted polymers preparation (NIPs), but without the template (cefalexin).

Instruments

In this study ion analyzer that used is (WTW model, Germany), a pH meter is (WTW model pH 720, Germany), and a saturated calomel electrode is (Gallenkamp, USA). The electrode CFX-MIP used was structure in the laboratory, and all potentiometric measurements were made at room temperature. The cefalexin-MIP electrode combined with the Ag-AgCl electrode, and reference electrode was 0.1 M cefalexin internal solution. 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 PVC tubing external diameter and pasted on polished end. The other PVC tubing direction was linked to electrode body, to make electrodes more sensitive by soaking in 0.1 M cefalexin solution for at least (2-3 hr) before the electrodes using.

Materials and Chemicals

- Standard cefalexin obtained from pharmaceuticals industries (IRAQ-SDI -Samarra).
- Cefex capsules 500mg Micro labs limited, India. AndCefalaxin capsules 250mg Aurobindopharma-MilpharmLtd,U.S.A.
- Plasticizers, Tri-oly phosphate (TOP) (99.5% purity), and di-octyl phthalate (DOP) (98.0% 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 cefalexin standard solution of 0.1 M, it's by dissolving 3.654 g from standard cefalexin in methanol and completed to 100 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, phosphor molybdic acid was prepared by dissolving (0.225 g, 0.022 g), respectively in distilled water and completed to 100 mL.
- For all interfering cations (K^+, Ca^{+2}, Al^{+3}) and some pharmaceutical additives such as methyl paraben, propyl paraben, tri sodium citrate 0.1 M stock solution prepared at ranged from10^{-6} -10^{-1} M which present the interfering ions were prepared and diluted to 100 mL.

Synthesis of membrane molecularly imprinted polymers electrode

As portrayed by Rafela and Felisminacefalexin membrane was arrested into the PVC tube, **(Stanley *et al.*, 2003)**. CFX-MIP of 0.036 g was mixed with plasticizers different 0.4 g

used, in this work such as DOP (electrode A1), TOP (electrode A2). After thatto have a clear viscous solution was acquired add 0.20 g powder PVC scattered on 7 ± mL of tetrahydrofuran with stirring. Then the solutions mixed with stirring until the mixture became matching. The mixture was casted into a glass ring (30-35) mm diameter and unwind on a glass plate and a filter ribbon was placed on top of the glass. Then the solvent allowed to evaporate according to room temperature more than 48 hr at least. The obtained membrane thickness was different from membrane to others; the thickness was about (0.4-0.7) mm. That membrane size was adequate to prepare electrodes.

Scanning electron microscope SEM

In scanning electron microscopy first scans all an electrons fine beam membrane surface. This causes many kinds of interactions generating different signals, and that also used in image formation. The SEM can be used to get an idea about the size, geometry, and distribution for membranes pore surface.

The morphological characteristics of the MIPs before and after the removal of the template membranes were analyzed by electron microscope scanning using Tokyo / Japan-JSM-6390 A to explain the variations between the SEM images of both the pre- and post-template MIPs obtained in proportion to the size and surface morphology of the polymer particles. SEM Analysis displayed highly ordered and organized pore structure for the molecular imprinted polymer surface and the cross section. Several papers showed that the imprinted molecular membranes known the template molecule effectively and transported it with good efficiency due to molecularly imprinted polymer porous structures. The ordered porous and cross-section on surface displays interaction sites, 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, Figure 2B) and (Figure 3A, Figure 3B). Micro emulsion polymerization gives very small particles size around (1.100-1.400) Mm and (0.900-1.200) Mm for 1-Vinyl imidazole polymer in both, MIPS can be distinguished in the related image. SEM analysis shows that the surface and cross-section molecular imprinted polymer have a highly ordered and normal pore structure that serves as the sites of interaction. (Figure 2A, 2B) shows that micro emulsion polymerization gives very small particle sizes for vinyl acetate (VA) polymer about 63.8 nm to 347.5 nm and for 1-vinylimidizol (VIZ) polymer between 190.3 nm and 542.5 nm.

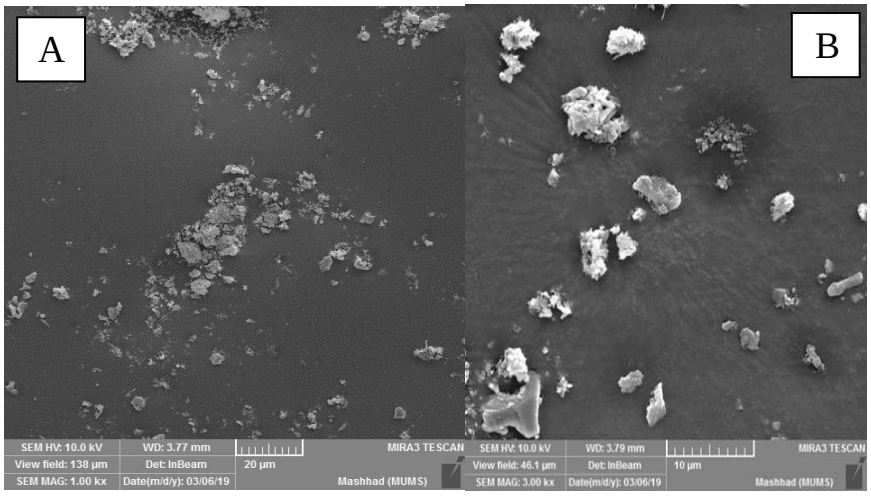

Figure (2):A. SEM of [CFX-MIP(VIZ)], B. [CFX-MIP(VA)] obtained by bulk polymerization before washing.

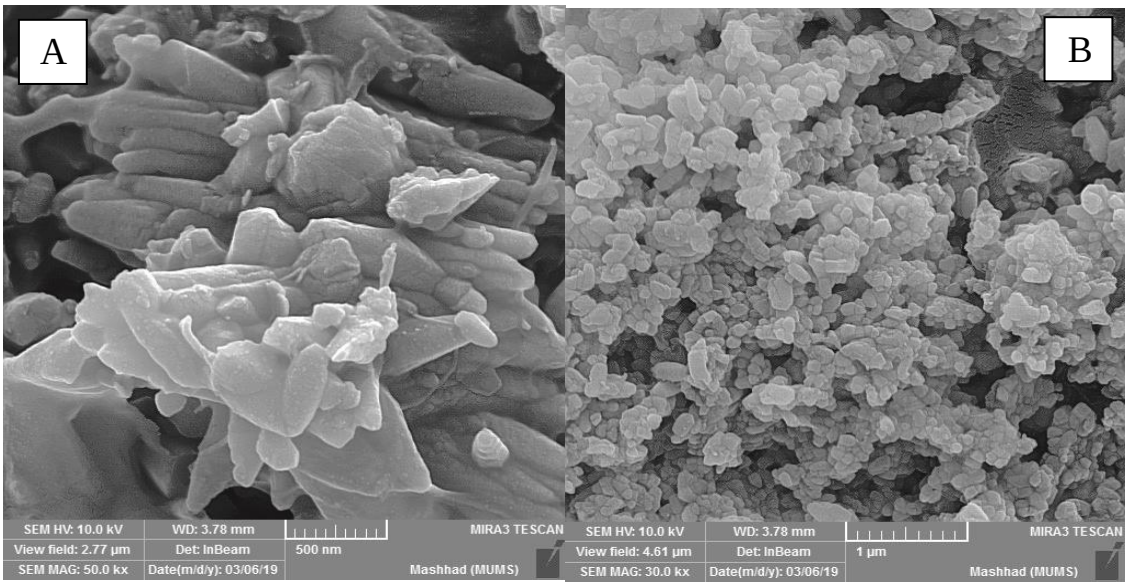

Figure (3):A. SEM of [CFX-MIP(VIZ)], B. [CFX-MIP(VA)] obtained by bulk polymerization after washing

RESULT AND DISSCUTION

The prepared membrane morphology using the PPHMIP1 before washing is presented in (Figure 3A) and after washing is shown in (Figure 3B). As seen in (Figure 2A) (before washing) reveals that the particles complex are formed in a regular spherical shape with an average about µm in diameter. In contrast, (Figure 3B) shows structure of MIP after washing that the formed particles look like a colloidal particle growing in a solution; this might occur due to the excess presence a DFS that form ionic atmosphere surrounding the complex and create double electric layers formation.

Construction of ion-selective electrodes

The electrode body building and the immobilization were completed as Mahajan *et al*., **(Mahajan & Sood 2007).** portrayed, cefalexin solution 0.1 M was filled in glass tube as an internal solution. It's a favorite to membrane immersing in 0.1 M a cefalexin standard solution for at least 3 hr. before measurements, which represents membrane electrode stipulations.

Preparation of pharmaceutical samples

Both cefalexin capsules bottles contents are from company cefex and cefalaxin, each capsules type contain on cefalaxin 500 mg and 250 mg, respectively. A specific amount of these was equal to a stock solution with 10^{-3}M concentration and transferred into a 50 mL calibrated flask and reminder volume was completed with distilled water.

Two of MIPs have been made by using the cefalexin (CFX) as the template, 1-vinyl imidazole (VIZ), and Vinyl acetate (VA) as monomers in addition to N, N-methylene bis acrylamide (MBAA) as cross linker and benzoyl peroxide as initiator. A plasticizer is an important element in an ISE membrane because it's provided harmony environment between polymer and other membrane constituents, practical when plasticizers using as a solvent for membrane, the ISE membrane using should be avoided leaching plasticizer; otherwise, it would effect on electrode performance over time. Four electrodes have been established based on PVC matrix, these plasticizers like Tri-oly phosphate (TOP), and di-octyl phthalate (DOP). All electrodes characteristics were studied based on CFX-MIP3 (A1, A2 membranes) and CFX-MIP6 (B1, B2 membranes), which included linearity range, correlation coefficients, detection

limit (M) and life time (day) respectively. The results that gained showed in (Table 1) and (Figure 4).

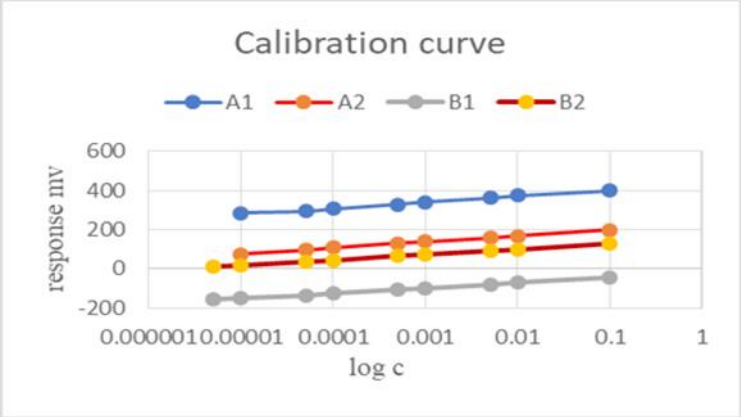

Figure (4): Calibration curve for CFX-MIP3 and CFX-MIP6 membranes electrodes.

Effect of pH on electrodes response

Studying pH effect on CFX membranes electrodes by prepared various concentrations of CFX (1×10-2, 1×10-3 and 1×10-4) M. To measure 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. To obtain the results we should add an appropriate volume of HCl/NaOH, as presented in (Table 2) and (Figure 5, 6). The variation in potentials at different pH values may happen due to the electrodes structure. This structure also distresses response and lifetime of electrodes.

Calculation by Multiple Standard Addition Method (MSA)

The concentrations used in the applied in this method (1×10^{-3} and 1×10^{-4}) are two cefalexin solutions to plot the antilog E/S (Y-axis) against volume of standard Cefalexin (X-axis). (Figure 7 and 8) represents the results of cefalexin Oride-MIP electrode based on different functional monomers and plasticizers.

Table (1): The characteristics of CFX-MIP electrode using two different a monomer and two different plasticizer.

Membrane composition	*CFX-MIP3 + DOP (A1)*	*CFX-MIP3 +TOP (A2)*	*CFX-MIP6 +DOP (B1)*	*CFX-MIP6 +TOP (B2)*
Slop (mV/decade)	-18.84	-18.48	-18.60	-19.47
Linearity range (M)	1×10^{-5}-1×10^{-1}	1×10^{-5}-1×10^{-1}	5×10^{-5}-1×10^{-1}	5×10^{-5}-1×10^{-1}
Correlation coefficient	0.9941	0.9899	0.9936	0.9837
Detection limit (M)	9×10^{-1}	7×10^{-1}	6×10^{-1}	8×10^{-1}
Life time (day)	6	8	5	7

Table (2): Working pH range for Cefalexin Select pH range.

Number and composition of MIPs	Membranes	Membrane composition	1×10^{-2}M	1×10^{-3}M	1×10^{-4}M
MIP3 CFX+1-VI+ MBAA	A1 A2	CFX-MIP3 +DOP CFX-MIP3 +TOP	4-8.5 6-8.5	3-7.5 5-8.5	5-8.5 5-8.5
MIP6 CFX+ VA+MBAA	B1 B2	CFX-MIP6+DOP CFX-MIP6 +TOP	7.5-9 5-9	4.5-9 5.5-7.5	5-7.5 7-9

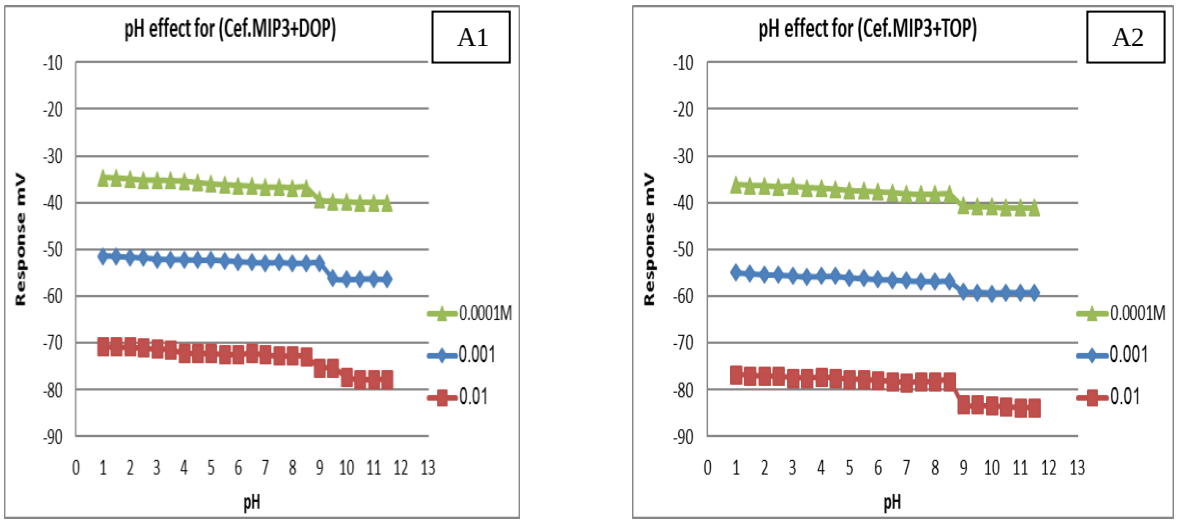

Figure (5): Effect of pH on the Cefalexin {CFX-MIP3 + DOP (A1) and CFX-MIP3 +TOP (A2)} electrodes at concentration 1×10^{-2}, 1×10^{-3} and 1×10^{-4}M.

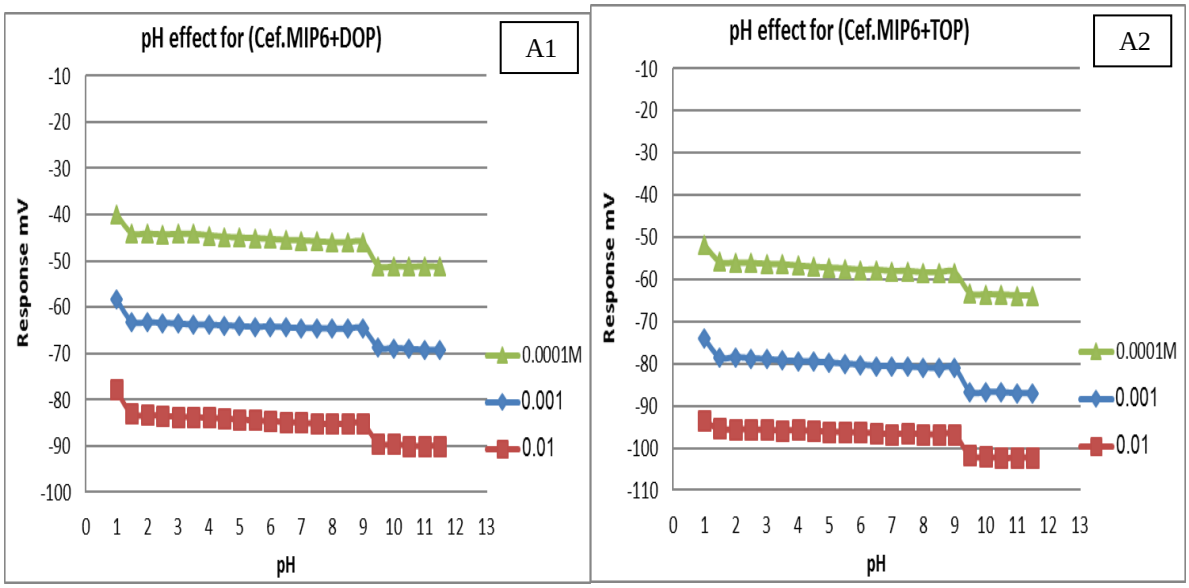

Figure (6): Effect of pH on the Cefalexin {CFX-MIP6 + DOP (A1) & CFX-MIP6 +TOP (A2)} electrodes at concentration 1×10^{-2}, 1×10^{-3} and 1×10^{-4}M.

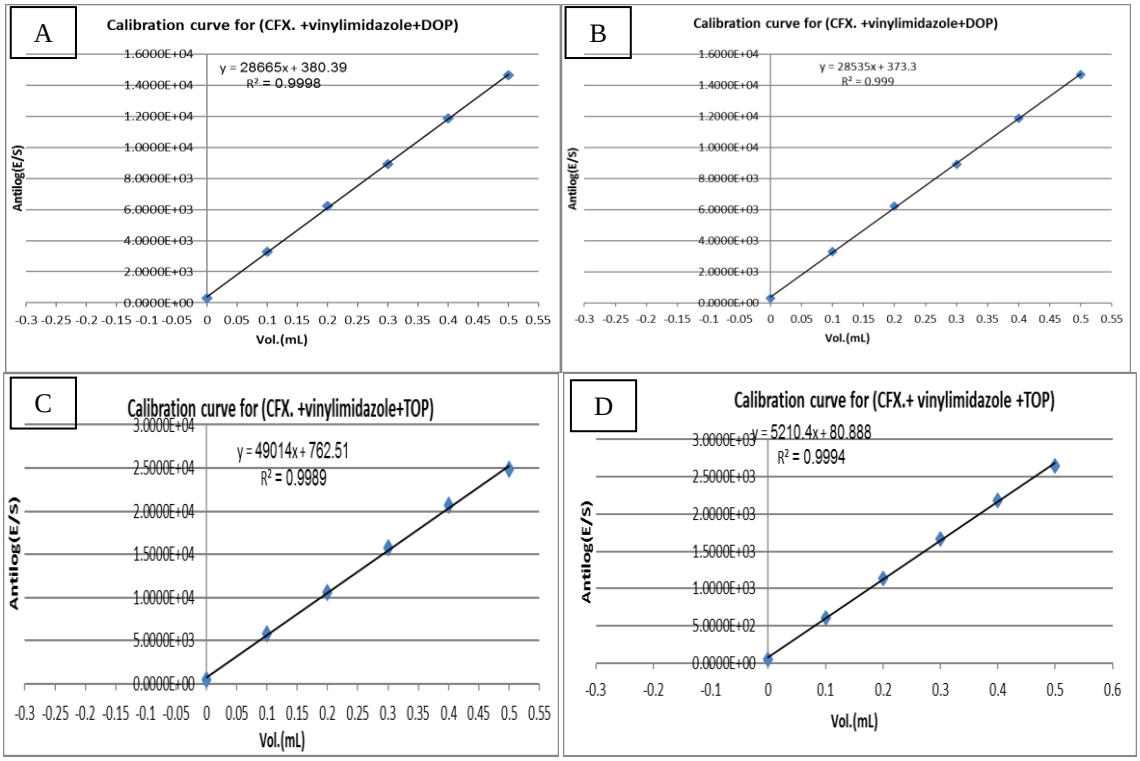

Figure (7): Antilog (E/S) against the volume of the added standard for the determination of cefalexin solution (1×10^{-3} and 1×10^{-4}) by MSA using (CFX–MIP3 + DOP) and (CFX–MIP3 + TOP) electrode respectively.

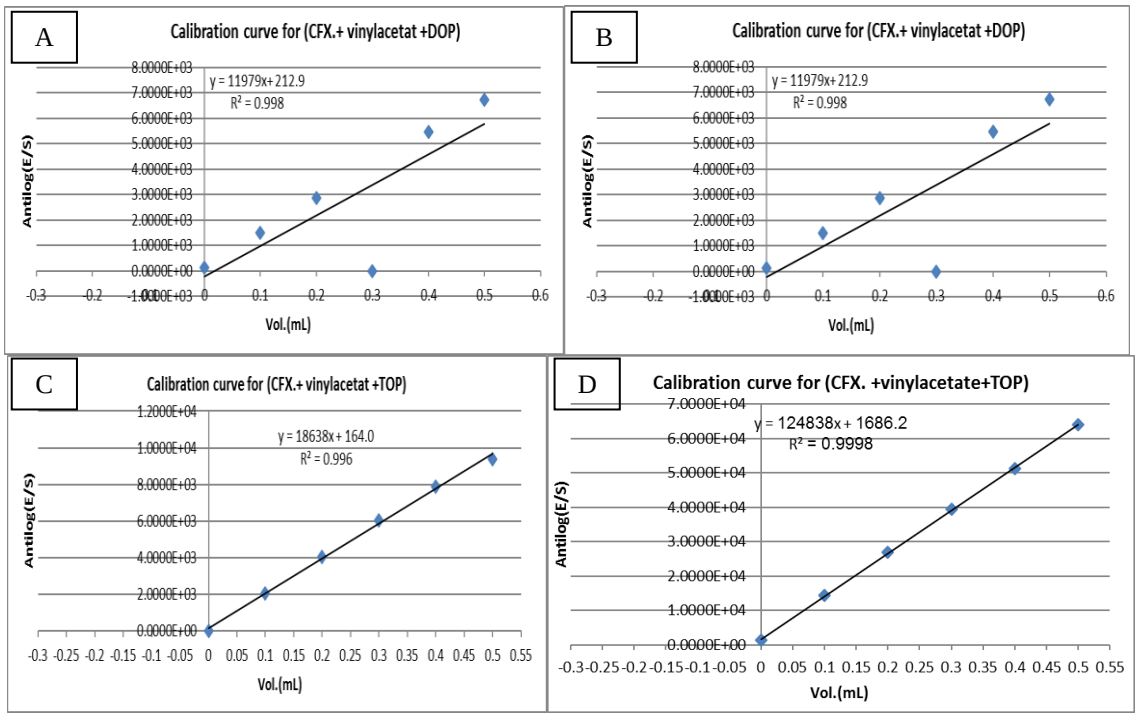

Figure (8): Antilog (E/S) against the volume of the added standard for the determination of cefalexin solution (1×10^{-3} and 1×10^{-4}) by MSA using (CFX–MIP6 + DOP) electrode and (CFX–MIP6 + TOP).

Titration methods (Titrimetry)

The measurement has depended in this method on changes, that to be a huge alteration in the electrode response to detect the titration end point. The procedure has been accomplished by using volumetric analysis of concentrations (1×10^{-3} and1×10^{-4}) M of Cefalexin against solutions (1×10^{-3} and1×10^{-4}) M of concentrations (PMA). The parameter results for RSD%, RC%, and RE% for all electrodes are listed in (Table 3).

Table (3): Cefalexin sample analyses by using titration method for CFX electrodes.

Electrode No.	**Concentration (M)**	
CEF-MIP3+DOP	Sample	Measured using PMA as titrant
	1×10^{-3} M	1×10^{-3}M
	RSD (%)	2.15
	RC (%)	101.55
	RE (%)	1.55
	1×10^{-4}M	1×10^{-4}M
	RSD (%)	2.89
	RC (%)	102.08
	RE (%)	2.08

Table (4): Cefalexin sample analyses by using titration method for CFX electrodes.

Electrode No.	**Concentration (M)**	
CEF-MIP3+TOP	Sample	Measured using PMA as titrant
	1×10^{-3} M	1×10^{-3}M
	RSD (%)	2.30
	RC (%)	102.36
	RE (%)	1.36
	1×10^{-4}M	1×10^{-4}M
	RSD (%)	3.63
	RC (%)	102.63
	RE (%)	2.68

Table (5): Sample analyses of pharmaceutical cefalaxin using CFX-MIP3+DOP electrode.

pharmaceutical	**Cefalaxin (Iraq)**			
	M.S.A	S.A.M	Direct method	Titration Method
Concentration prepared	1×10^{-3}	1×10^{-3}	1×10^{-3}	1×10^{-3}
found	1.011×10^{-3}	1.0115×10^{-3}	1.0259×10^{-3}	1.0262×10^{-3}
RC (%)	101.10	101.62	102.58	102.63
RSD (%)	……	2.44	2.94	3.63
RE (%)	1.10	1.62	2.58	2.63
pharmaceutical	M.S.A	S.A.M	Direct method	Titration Method
Concentration	1×10^{-4}	1×10^{-4}	1×10^{-4}	1×10^{-4}
prepared	1.0165×10^{-4}	1.0188×10^{-4}	1.0121×10^{-4}	1.0247×10^{-4}
Found	…..	2.35	3.18	3.44
RSD (%)	101.64	101.88	102.12	102.49
RC (%)	1.64	1.88	2.12	2.49

Table (6): Sample analyses of pharmaceutical cefalaxin using CFX-MIP3+DOP electrode.

pharmaceutical	**Cefalexin (Indea)**			
	M.S.A	S.A.M	Direct method	Titration Method
Concentration prepared	1×10^{-3}	1×10^{-3}	1×10^{-3}	1×10^{-3}
found	1.0136×10^{-3}	1.0037×10^{-3}	1.0129×10^{-3}	1.0158×10^{-3}
RC (%)	101.35	100.37	101.30	101.55
RSD (%)	……	1.74	2.18	2.15
RE (%)	1.35	0.37	1.30	1.55
pharmaceutical	M.S.A	S.A.M	Direct method	Titration Method
Concentration		1×10^{-4}	1×10^{-4}	1×10^{-4}
prepared	1×10^{-4}	1.0137×10^{-4}	1.0120×10^{-4}	1.0208×10^{-4}
Found	1.0116×10^{-4}	3.5	2.73	2.89
RSD (%)	…..	101.37	101.97	102.08
RC (%)	101.11	1.37	1.97	2.08

Table (7): Sample analyses of pharmaceutical cefalaxin using CFX-MP3+TOP electrode.

pharmaceutical	**Cefalexine (Iraq)**			
	M.S.A	S.A.M	Direct method	Titration Method
Concentration prepared	1×10^{-3}	1.0037×10^{-3}	1.0129×10^{-3}	1.0158×10^{-3}
found	1.0148×10^{-3}	1.0199×10^{-3}	1.0276×10^{-3}	1.0291×10^{-3}
RC (%)	101.48	101.99	102.76	102.91
RSD (%)	……	4.12	3.78	4
RE (%)	1.48			
pharmaceutical	M.S.A	S.A.M	Direct method	Titration Method
Concentration	1×10^{-4}	1×10^{-4}	1×10^{-4}	1×10^{-4}
prepared	1.0190×10^{-4}	1.0296×10^{-4}	1.0292×10^{-4}	1.0319×10^{-4}
Found	…..	2.23	3.89	4.37
RSD (%)	101.90	102.16	102.92	103.19

Table (8): Sample analyses of pharmaceutical cefalaxin using CEF-MIP3+TOP electrode.

pharmaceutical	**Cefalexine (Iraq)**			
	M.S.A	S.A.M	Direct method	Titration Method
Concentration prepared	1×10^{-3}	1×10^{-3}	1×10^{-3}	1×10^{-3}
found	1.0179×10^{-3}	1.0205×10^{-3}	1.0248×10^{-3}	1.0263×10^{-3}
RC (%)	101.79	102.05	102.48	102.63
RSD (%)	……	0.99	3.32	3.63
RE (%)	1.79	2.05	2.48	2.63

pharmaceutical	M.S.A	S.A.M	Direct method	Titration Method
Concentration	1×10^{-4}	1×10^{-4}	1×10^{-4}	1×10^{-4}
prepared	1.0173×10^{-4}	1.0225×10^{-4}	1.0266×10^{-4}	1.0291×10^{-4}
Found	…..	3.01	3.63	4
RSD (%)	101.73	102.25	102.66	102.91
RC (%)	1.73	2.25	2.66	2.91

Table(9): Sample analyses of pharmaceutical cefalaxin using CEF-MIP6+DOP electrode.

pharmaceutical	**Cefalexine (Iraq)**			
	M.S.A	S.A.M	Direct method	Titration Method
Concentration prepared	1×10^{-3}	1×10^{-3}	1×10^{-3}	1×10^{-3}
found	1.0105×10^{-3}	1.0213×10^{-3}	1.0223×10^{-3}	1.0225×10^{-3}
RC(%)	101.05	102.13	102.23	102.25
RSD(%)	……	3.53	2.62	3.11
RE(%)	1.05	2.13	2.23	2.25
pharmaceutical	M.S.A	S.A.M	Direct method	Titration Method
Concentration prepared	1×10^{-4}	1×10^{-4}	1×10^{-4}	1×10^{-4}
Found	1.0176×10^{-4}	1.0204×10^{-4}	1.01238×10^{-4}	1.0253×10^{-4}
RSD(%)	…..	2.39	3.32	3.48
RC(%)	101.76	102.04	102.38	102.53
RE(%)	1.76	2.04	2.38	2.53

Table (10): Sample analyses of pharmaceutical cefalaxin using CEF-MIP6+TOP electrode.

pharmaceutical	Cefalaxin (Indea)			
	M.S.A	S.A.M	Direct method	Titration Method
Concentration prepared	1×10^{-3}	1×10^{-3}	1×10^{-3}	1×10^{-3}
found	1.0179×10^{-3}	1.0294×10^{-3}	1.030×10^{-3}	1.0349×10^{-3}
RC (%)	102.53	102.94	103.31	103.49
RSD (%)	……	3.82	3.32	4.78
RE (%)	2.53	2.94	3.31	3.49
pharmaceutical	M.S.A	S.A.M	Direct method	Titration Method
Concentration prepared	1×10^{-4}	1×10^{-4}	1×10^{-4}	1×10^{-4}
Found	1.0273×10^{-4}	1.0298×10^{-4}	1.0310×10^{-4}	1.0319×10^{-4}
RSD (%)	…..	4.20	3.63	4.37
RC (%)	102.73	102.98	103.03	103.19
RE (%)	2.73	2.98	3.03	3.19

CONCLUSION

In this analysis, four electrodes were prepared on the basis of the MIP method using two monomers (VA, VIZ) and two separate plasticizers (DOP, TOP), as it was found that the

interaction between the template and the monomer was non-covently, so that the CFX drug was readily extracted to form a selective cavity for commercial CFX estimation.

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