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المجلة العراقية لبحوث السوق وحماية المستهلك

ELECTROCHEMICAL PREPARATION OF A MOLECULAR IMPRINTED POLYMER ELECTRODE FOR ESTEMATION OF ASPIRIN USING TWO DIFFERENT FUNCTIONAL MONOMERS.

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ABSTRUCT

For aspirin estimated, a molecularly imprinted polymer MIP-ASP electrodes were generated by electro-polymerization process, the electrodes were prepared by combining the template (aspirin) with (vinyl acetate (VA), 1-vinylimidizole (VIZ) as a functional monomer and N, N-methylene bisacrylamide (MBAA) as crosslinkers using benzoyl peroxide (BPO) as an initiator. The efficiency of the membrane electrodes was analyzed by differential pulse voltammetry (DPV). Four electrodes were synthesized using two different plasticizers, di-butyl sebacate (DBS), di-octyl phthalate (DOP) in PVC matrix. Scanning electron microscopy (SEM) was used to describe the generated MIP, studying the electrodes properties, the slope, detection limit, and life time and linearity range. The effect of PH and interferes on the efficiency of the MIP electrode was investigated. The study has shown that the molecularly imprinted electrodes have high sensitivity and responsiveness to aspirin. 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 aspirin with correlation coefficients are about (0.9974, 0.9966, 0.9938 and 0.9961) with slops value of (-21.41, -17.67, -17.47 and -18.67) and the detection limit for all electrodes ranging from (7.5×10-5-1×10-4) M. The molecularly imprinted electrode exhibited a good response with highly reproducible and no effect on interferes frequently available in pharmaceutical formulations. The approach employed is easy and fast. Also ASP membranes get a limited time of response, excellent mechanical stability, removable and are easy to construct.

Keywords: molecularly imprinted electrochemical sensors (MIECS), Aspirin (ASP), potentiometric method, vinyl acetate (VA) monomer, 1-vinylimidizol (VIZ) monomer.

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التحضير الكهروكيميائي لقطب بوليمر مطبوع جزيئيا لتقدير الاسبرين وباستخدام وحدتين وظيفيتين مختلفتين

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الخلاصة

لتقدير الأسبرين، تم إنشاء أقطاب بوليمرية مطبوعة جزيئيا MIP-ASP عن طريق *Electro-polymarization* ، تم تحضير الأقطاب الكهربائية عن طريق الجمع بين القالب (الأسبرين) مع (الفينيلأسيتات (VA)، 1-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 ثنائي- بوتيلسيبيكيت (DBS)، وثنائي أوكتيلفثاليت (DOP) في مصفوفة PVC، وتم 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 للأسبرين. وكانت قيم الـ DPV هي خطية اعتماد على تركيز الأسبرين وتم الحصول على منحنى خطي ضمن حدود M (1×10^{-4}-5×10^{-1})مولاري من الأسبرين مع معاملات الارتباط حوالي (0.9974 ، 0.9966 ، 0.9938 و 0.9961) بقيمة انحدار تبلغ (-21.41 ، -17.67 ، -17.47 و -18.67) وحد الكشف لجميع الأقطاب الكهربائية يتراوح من (1×10^{-4}-7.5×10^{-5})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 ASP على وقت استجابة محدود، واستقرار ميكانيكي ممتاز، وقابلة للإزالة وسهلة التركيب.

الكلمات المفتاحية: أجهزة الاستشعار الكهروكيميائية المطبوعة جزيئيًا (MIECS)، الأسبرين (ASP)، طريقة قياس الجهد، مونومرأسيتاتالفينيل (VA)، مونومر 1-فينيل ايميدزول(VIZ).

INTRODUCTION

An advance in molecularly imprinted polymers (MIPs) is a useful method to a preparatory work of the polymeric materials with active sites. **(Lata *et al.*, 2015)**. MIPs are polymers that are manufactured to create cavities with attraction to a selected "template" molecule within the polymer chains. They have been prepared by complexing the target (template) with the FM, whether by covalently or non-covalently bonding, accompanied by polymerization with large quantities crosslink's to establish a highly cross linked polymeric network. When the target-molecule is extracted from of the polymeric matrix , different recognizing locations are identified which are comparable to the target in terms of size, shape and function **(Meier & Mizaikoff, 2010)**. MIPs have been used in various applications, including chromatography **(Li *et al.*, 2014)**, capillary electrophoresis chromatography **(Rutkowska *et al.*, 2018)**, quartiz crystals of micro-balance **(EL-Sharif *et al.*, 2015)**, membranes separation **(Balouch *et al.*, 2019)**, SPE **(El Nashar *et al.*, 2017; He *et al.*, 2015)** and the sensors of biomimetic **(Huang *et al.*, 2018; Lahcen & Amine, 2019; Malitesta *et al.*, 2017)**. MIPs have several benefits, including high specificity and selectivity to target molecules, greater chemical and mechanical stabilization, insoluble in DW and most organic solvents. In additional, the MIP have easily synthesis and have good mechanical properties, reliability for pressures and temperatures, and thus are cost-effectively and suitable to applicable for harmful chemicals **(Al-Bayati & Aljabari, 2016; N. Zhang *et al.*, 2019)**MIPs are the sensing elements of a molecular imprinting electrochemical sensor (MIECS) which are molecularly imprinted. The sensor could specifically recognise of the target molecules depending upon this cavities (active site) in the molecular structure of imprinting polymer.

Once the template have been extracted, the active site representing the spatial configuration of a target molecules will be obtained as well as the electrochemical response has been received because when MIP is associated with a particular template the electrosignal was recorded depending on the active site, as well as the targeted molecule concentrations can be estimated**(Crapnell *et al.*, 2019; Jin *et al.*, 2015; Varghese *et al.*, 2019)**. MIECS have many characteristic includes: high selectivity, simplest techniques, lower costs, low D.L, highly stable. The combination of both the template molecules and the cavities can also be easily achieved and is carefully applicable even with harmful chemical materials. Thus, MIECS was used for optical and electrochemical applicable **(Al-Bayati & Abd, 2017; Al-Bayati & Al-Safi, 2018; D'Aurelio *et al.*, 2020; Momeneh & Gholivand, 2018; Tadi & Motghare, 2016).** The utilization of molecular imprinting techniques have increased significantly in recent years, thus illustrating magnificently the ability of MIP model for detection toward the target molecules**(Bates *et al.*, 2017; Marć *et al.*, 2018).**

As in present study, four of the MIPs have been manufactured as recognizing materials using [Vinylacetate (VA), 1-Vinylimidizol (VIZ)] as functional monomer, N, N-methylene bis-acrylamide (MBAA) is a crosslinkers also benzoyl peroxide (BPO) as an initiators using methanol as porogen solvent. The efficiency of the MIPs was tested using rebinding equilibrium assays. The highest efficiency of the MIP was selected as the identification substance in PVC membrane for the estimation of aspirin (ASP) in pharmacological samples.

Aspirin (ASP) is widely used in pharmaceutical formulations as an analgesic and antipyretic agent for relieving headaches, fever, muscle pains and inflammation severe arthritis. so the wide use of ASP had led to the therapeutic intoxication due to overdose , which can be found in individuals with chronic inflammatory diseases and routinely take ASP **(Kan *et al.*, 2009; Q. Zhang *et al.*, 2020)**(Figure 1) shown the aspirin structure. The aims of this research are studies the response of the MIP-sensor in presence / absences of interferences and record the analysis of the electro-chemical sensors for the estimation of ASP using MIP-sensor electrodes.

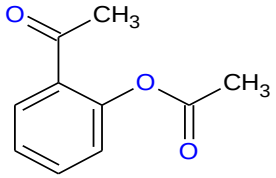


Figure (1): Aspirin structure**.**

MATERIALS AND METHODS

The standard of aspirin was gained from of the government drug manufacturer (IRAQ-SDI-Samara). Aspirin tablets (100 mg) Chewable tablet, acetylsalicylic acid ((SDI)-IRAQ and Memphis/Bayer) were purchased from local pharmacies.Plasticizers: (DBS) (97.0% purity) and (DOP) (99.5% purity), were purchased from Sigma Aldrich. Other chemicals and reagents materials were obtained from Fluka, BDH and Sigma Aldrich.

Instruments

In this work, We use potentiometric measured data by digital voltmeter (PH 211 HANA devices). An analyzer (WTW model, Germany), SCE (Gallenkamp, USA), pH meter (WTW model PH 720, Germany). UV-VIS dual-Beam system (UV-1650 PC) SHIMADZ (Japan), computer interfaced by a SHIMADZU UV investigate system (version 1.10), SHIMADZU FT-IR,-8000 (Japan), Scanning Electrons Microscopic (SEM) [JSM-6390A] (Tokyo, Japan) and sensitively balance (Electronically balance ACS120-4 Kern &Sohn GmbH, Germany). A quality of the electrodes has been monitored by measuring the potential of ASP solutions

ranging from 5×10^{-5} to 1×10^{-1} M at room temperature. The accuracy of electrode activity was measured and then the potential was registered after the internally and externally solution arrived to the equilibration.

Preparation of standard solutions for ISE study

100 mL of 0.1 M standard solution for aspirin was prepared by dissolving 1.802 g of aspirin in methanol. The ASP solutions ranged from (1×10^{-5}-1×10^{-1}) M in 100 mL, also the interferences ion (K^{+}, Ca^{+2}, Al^{+3}) was prepared ranging from (1×10^{-5}-1×10^{-1}) M in 100 mL volumetric flask and 100 mL of each (methyl paraben, propyl paraben, tri sodium citrate) interferences solution was prepared from (1×10^{-5}-1×10^{-1}) M of a stock solution of 0.1 M interference.

Molecular imprinting polymer synthesis

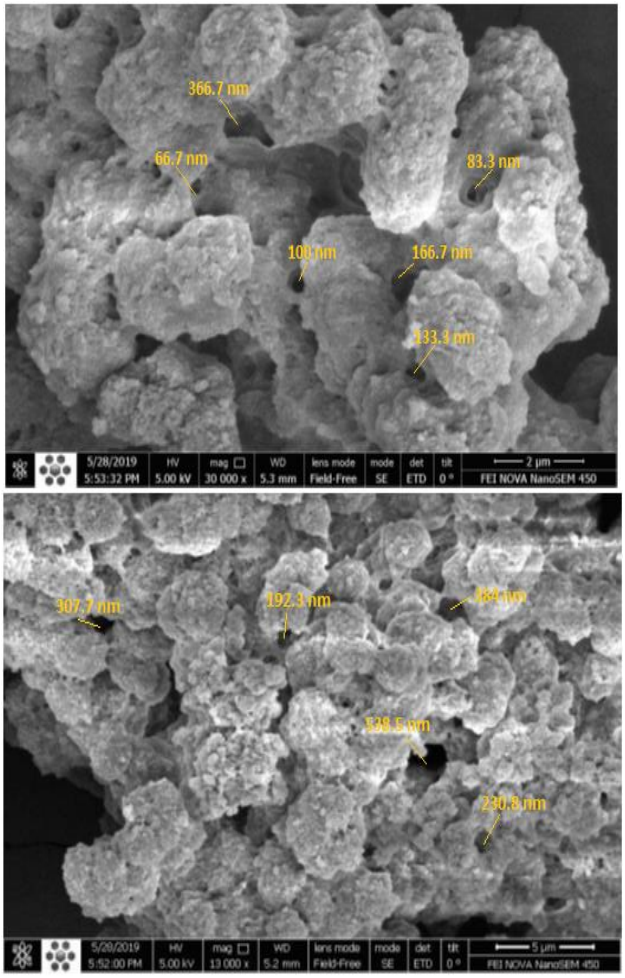
The first aspirin molecularly imprinted polymer (ASP-MIP_1) prepared by mixed 0.5 mmol (0.0901 g) from aspirin then mixed with 3 mmol (0.26 g) vinyl acetate (VA) as the monomer, after that added 15 mmol (2.313 g) N,N-methylene bis-acrylamide (MBAA) to the solution as the cross-linker, followed that added (0.32 g) benzoyl peroxide as the initiator. All these materials were dissolved in 5±mL methanol (CH_3OH) except the initiator have dissolved in 3 Ml chloroform. While the second aspirin molecularly imprinted polymer (ASP-MIP_2) were achieved by mixed 0.4 mmol (0.0721 g) from aspirin as the template, 2.4 mmol (0.226 g) 1-vinylimidizol (VIZ) as the monomer, 12 mmol (1.85 g) N,N-methylenbisacrylamide (MBAA) act as crosslinkers also (0.3 g) benzoyl peroxide as the initiator which dissolved in 5mL 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 removeoxygenfrom the solution. After that, the solution was put at 60˚C in a water bath. 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 acetonitrile/ CH_3COOH (18:2 v/v) to remove the template from MIP. The polymer was dried for (42-75) hours at room temperature, crushed and ground the polymers by mortar and pestle and sieve to get 125 µm particle size (using 125µm mesh sieve); after dried completely at room temp., has been used in the membrane of the selective sensors as an active substance. To fabricate of electrode, The PVC tubing (1-2 cm long) was placed that on a glass slide and soaking it with THF. Similar to an average thickness of the PVC tubing, the membranes also was cut and pasted onto the end tube other end of that was connected to an electrode of Ag-AgCl.

Preparation of pharmaceutical samples.

The mortar has used to create the powder of the pharmaceutical tablets. There were two different types of ASP-tablets used it to estimate the molarity concentration of ASP-drugs. An appropriate weight of powder was then taken to prepare of (1×10^{-3} and 1×10^{-4}) M from the pharmaceutical sample solutions. Suitable quantity of methanol has been used to dissolve pharmaceutical samples and to complete volumes of up to 100 mL.

Scanning Electron Microscope (SEM)

A morphological characteristics of the MIPs before and after template removal membranes was evaluated by scanning the electron microscope using Tokyo / Japan-JSM-6390 A, in order to show the differences between both the SEM image of both the MIPs before and after the template obtained in proportion to the size and surface morphology of a polymeric particles. SEM analysis indicates that molecular imprinted polymer in surface and in cross-section, had a highly ordered and regular pore structure which serves as the sites of interaction, in (Figure 2a and b) can be seen that micro emulsion polymerization gives very small particles size around 66.8 nm to 366.7 nm for Vinyl acetate (VA) polymer and 192.3 nm to 538.5 nm for vinylimidizol (VIZ) polymer.



a b

Figure 2:. a. SEM of [ASP-MIP(VA)], b. [ASP-MIP(VIZ)] obtained by bulkpolymerization.

RESULTS AND DISCUSSION

Four MIP membranes are prepared using two different monomers VA and VIZ with PVC matrix and two different plasticizers DBS and DOP, the ions selective polymer membrane is one of the most crucial components of ISEs. It isolates the internal reference solution from the external analytical sample solution. Polymeric membranes must have selectivity for different analyte ions, un-porous, insoluble in water and mechanically stable, based on the natural of the membrane material used. Other critical components of an ISE assembly are the internally and externally reference electrodes. Collection consisting of both reference electrodes and also the polymeric membrane is referred to as cell the characteristic of these membranes were studied, including: slope, detection limit, linearity, life time and the response to the Nernstian equation were investigated; the results in (Table, 1) indicated that both monomer and both plasticizers can be used for preparing effective MIP for ASP.

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

Membranes no.	Membrane composition	Parameter			
		Slope mv/decade	Correlation coefficient (r)	Linearity range (M)	Detection limit/ M
I	ASP-MIP_1 (VA+MBAA+DBS)	-21.41	0.9974	1×10^{-4}-1×10^{-1}	7.5×10^{-5}
II	ASP-MIP_1 (VA+MBAA+DOP)	-17.67	0.9966	1×10^{-4}-1×10^{-1}	8.0×10^{-5}
III	ASP-MIP_2 (VIZ+MBAA+DBS)	-17.47	0.9938	5×10^{-4}-1×10^{-1}	8.5×10^{-5}
IV	ASP-MIP_2 (VIZ+MBAA+DOP)	-18.67	0.9961	5×10^{-4}-1×10^{-2}	1.0×10^{-4}

Infrared spectroscopy (FTIR- Analysis)

The FTIR is a commonly utilized method of substance characterisation. The spectral generated from of the analysis provides the specific samples their identities. The peak frequency of absorption relate to signature vibration of binds between all the atoms that create up the product. The FTIR spectrum is therefore a substance characteristics and allows accurate recognition.The listed in (Table, 2& 3) showed a band that before/after removal ASP-template from MIP_1& MIP_2 respectively.

Table (2). The FT-IR spectra for ASP-VA polymer before/after removal clop-template.

F.G.	ASP.	ASP–VA (MIP_1) before ASP removal	ASP–VA (MIP_1) after ASP removal
O-H str.	3200-2500	3384	3398 (enol)
C-H arom.	3016	3060	-
R-C=O.	1755	1720	-
COOH	1691	1654	-
C=C arom.	1604	1521	-
C=C aliph.	-	-	1527
COOR	-	1733	-

From this table can be seen (before ASP removal) that the characteristically peak at ~1733 cm^{-1} is attributable to vibrational mode of -COOR and the vibration version of amide N-C=O is allocated at ~1654 cm^{-1} these notes indicated to fact that the interaction occurred between the template (ASP) and the monomer (VA), while after ASP removed the detected peak characteristics are missing in carboxylic spectra at ~1654 cm^{-1}, carbonyl group at ~1720 cm^{-1} and also missing the absorption band of C=C at ~1521 cm^{-1}. The results indicated that the height contrast of imprinted polymer FT-IR spectra before and after template removal proves that ASP-template has been fully extracted from MIP_1 in the extraction stage by soxhlet.

Table (3): The FT-IR spectra for ASP-VIZ polymer before/after removal ASP-template

F.G.	ASP.	ASP-VIZ (MIP_2) before ASP removal	ASP-VIZ (MIP_2) after ASP removal
O-H str.	3200-2500	3300-3000	-
C-H arom.	3016	3060	3058
C-H aliph	2974-2833	2952-2866	2948
R-C=O.	1755	-	-
COOH	1691	1658	-
C=C arom.	1604	-	1525
N-C=O	-	1627	1654

The results indicate that the strongest two peaks are missing at ~1691 cm^{-1} and ~1755 cm^{-1} for carbonyl group stretching C=O and C=C aromatic stretching respectively, while the characteristically peak appears at ~1627 cm^{-1} due to interaction between the ASP-template and the VIZ-monomer, However when the ASP-template removed after washing noticed that the carbonyl group at ~1658 cm^{-1} and the hydroxyl group at ~3300 cm^{-1} are missing, that also indicated the template are completely extracted in the soxhlet extraction stage from MIP_2.

Effect of pH on ASP-electrodes

The pH dependency of the electrode sensor membrane was measured at a pH range of 1× (10^{-4}, 10^{-3} and 10^{-2}) M aspirin concentrations (Figure 3). PH modifications were made with (HCl or NaOH) solutions. The results in (Table, 4), indicate that the potentials slightly change and remain constant from ~pH (3.0 to 9.0). Therefore, this range can be considered as the pH of working electrode senses. The behaviors of this membrane can be explained as follow: a) the pKa of aspirin is about 3.0, i.e. at acidic pH, observed that the potential will be relatively high at this range; this might be because the membrane can responds to H^+ activity. b) at higher pH 9.0, it becomes increasingly dissociated for this explanation we have noticed a decline in potential.

Table (4): Effective pH ranges used for ASP-selective electrodes.

Membranes no.	Membrane composition	PH rang		
		1×10^{-2}	1×10^{-3}	1×10^{-4}
I	ASP-MIP_1 (VA+MBAA+DBS)	2.5-9.0	3.0-8.5	2.5-9.5
II	ASP-MIP_1 (VA+MBAA+DOP)	3.0-9.0	2.5-9.5	4.0-9.5
III	ASP-MIP_2 (VIZ+MBAA+DBS)	3.5-9.0	3.0-9.0	3.5-10.0
IV	ASP-MIP_2 (VIZ+MBAA+DOP)	3.0-9.5	2.5-9.5	3.0-9.0

Selectivity of ASP-electrodes potentiometric

The influence of interferences on the electrods-response behavior is usually described as the selectivity coefficients. So the K_{pot} selectivity coefficient of MIP-sensor's was analyzed using the separation solution method (SSM) and Matched Potential Method (MPM). The measured by SSM methods depend on equation of the Nickolsky-Eisenman but the SSM methods does have some disadvantages in line with interference ions (unequal charges) with non-Nernstainbehavior. Thus, a similar procedure referred to as [Matched Potential Method (MPM)] was preferred, in specific, as the primary or interference ion does not obey on the

Nernst response, or when the ions concerned is different in charge. As seen from results in (Table 5 and 6) the selectivity coefficients achieved for all prepared electrode sensors, that most of these compounds did not interfere with the response of the electrode sensors membrane.

Table (5): Result of selectivity coefficients for some interfering species using SSM for MIP_1 with different plasterer.

Interfering ions	Concentrations of Aspirin (MIP1+DBS) M: Concentrations of interference ions (M)													
	0.1		0.01		0.005		0.001		0.0005		0.0001		0.00005	
	E_B (mV)	$K_{A,B}$	E_B (mV)	$K_{A,B}$	E_B (mV)	$K_{A,B}$	E_B (mV)	$K_{A,B}$	E_B (mV)	$K_{A,B}$	E_B (mV)	$K_{A,B}$	E_B (mV)	$K_{A,B}$
K^+	-151.4	0.0078	-146.8	0.041	-143.2	0.0433	-136.6	0.131	-132.2	0.197	-127.4	0.502	-124.3	0.781
Ca^{2+}	-157.1	0.0046	-150.4	0.006	-149.3	0.0059	-147.9	0.014	-144.1	0.016	-142.5	0.025	-138.2	0.025
Al^{3+}	-156.3	0.0029	-153.2	0.0038	-152.6	0.0035	-150.1	0.0056	-148.7	0.007	-147.3	0.009	-145.8	0.011
M.P.	-131.7	0.0009	-130.5	0.0071	-129.4	0.0098	-127.6	0.0498	-127.3	0.116	-126.7	0.466	-126.4	0.979
P.P.	-133.8	0.0012	-131.6	0.008	-130.4	0.0109	-128.9	0.0572	-126.6	0.108	-124.2	0.356	-120.5	0.519
T.S.C.	-134.6	0.0003	-133.9	0.0005	-133.2	0.0004	-132.5	0.0008	-131.7	0.001	-129.7	0.001	-129	0.002
Interfering ions	Concentrations of Aspirin (MIP1+DOP) M: Concentrations of interference ions (M)													
	0.1		0.01		0.005		0.001		0.0005		0.0001		0.00005	
	E_B (mV)	$K_{A,B}$	E_B (mV)	$K_{A,B}$	E_B (mV)	$K_{A,B}$	E_B (mV)	$K_{A,B}$	E_B (mV)	$K_{A,B}$	E_B (mV)	$K_{A,B}$	E_B (mV)	$K_{A,B}$
K^+	-241.4	0.0105	-239.2	0.071	-238.8	0.194	-223.4	0.0996	-220.1	0.174	-219.7	0.617	-217.5	0.878
Ca^{2+}	-238.7	0.0023	-236.4	0.005	-234.1	0.007	-231.8	0.0094	-230.3	0.015	-229.6	0.022	-226.4	0.02
Al^{3+}	-235.5	0.001	-232.1	0.001	-230.4	0.002	-229.4	0.0022	-226.1	0.002	-225.5	0.003	-224.7	0.003
M.P.	-231.7	0.003	-229.4	0.02	-226.4	0.038	-224.1	0.1091	-221.9	0.221	-217.7	0.476	-214.2	0.571
P.P.	-230.7	0.0026	-227.4	0.015	-225.3	0.033	-221.8	0.0809	-220.7	0.189	-217.5	0.464	-215.8	0.703
T.S.C.	-233.7	0.0008	-230.1	0.001	-225.5	0.001	-224.3	0.0011	-221.2	0.001	-219.8	0.001	-219.1	0.001

Table (6). Result of selectivity coefficients for some interfering species using SSM for MIP_2 with different plasterer.

Interfering ions	Concentrations of Aspirin (MIP2+DBS) M: Concentrations of interference ions (M)													
	0.1		0.01		0.005		0.001		0.0005		0.0001		0.00005	
	E_B (mV)	$K_{A,B}$	E_B (mV)	$K_{A,B}$	E_B (mV)	$K_{A,B}$	E_B (mV)	$K_{A,B}$	E_B (mV)	$K_{A,B}$	E_B (mV)	$K_{A,B}$	E_B (mV)	$K_{A,B}$
K^+	-90	0.0007	-54.3	5×10^{-5}	-35.7	6×10^{-6}	-28.2	1.5×10^{-5}	-22.4	1×10^{-5}	-21.5	6×10^{-5}	-16.6	9×10^{-5}
Ca^{2+}	-81.1	7×10^{-5}	-63.4	2×10^{-5}	-40	8×10^{-7}	-23	2.4×10^{-7}	-24.6	4×10^{-7}	-24.5	9×10^{-7}	-21.7	1×10^{-6}
Al^{3+}	-73.6	2×10^{-5}	-50.6	1×10^{-6}	-48.1	9×10^{-7}	-42.4	9.6×10^{-7}	-37.9	6×10^{-7}	-31.3	5×10^{-5}	-29.7	7×10^{-7}
M.P.	-101.2	0.003	-85.3	0.003	-84.2	0.0036	-75.5	0.00752	-71.4	0.0082	-63.6	0.0155	-61.8	0.0347
P.P.	-79.8	0.0002	-70.4	0.0004	-67.5	0.0004	-60.2	0.001	-54.6	0.0009	-51.5	0.0032	-49.7	0.007
T.S.C.	-79.6	4×10^{-5}	-70.6	2×10^{-5}	-64.1	7×10^{-6}	-55.4	5.3×10^{-6}	-50.9	3×10^{-6}	-45.3	3×10^{-6}	-41.2	3×10^{-6}
Interfering ions	Concentrations of Aspirin (MIP2+DOP) M: Concentrations of interference ions (M)													
	0.1		0.01		0.005		0.001		0.0005		0.0001		0.00005	
	E_B (mV)	$K_{A,B}$	E_B (mV)	$K_{A,B}$	E_B (mV)	$K_{A,B}$	E_B (mV)	$K_{A,B}$	E_B (mV)	$K_{A,B}$	E_B (mV)	$K_{A,B}$	E_B (mV)	$K_{A,B}$
K^+	-112.8	8.7×10^{-8}	-93.9	9.6×10^{-8}	-91.1	8.5×10^{-8}	-85.7	2.8×10^{-7}	-84.2	6.1×10^{-7}	-80.7	1.5×10^{-6}	-77.3	2.1×10^{-6}
Ca^{2+}	-116.3	4.2×10^{-8}	-106	4.3×10^{-8}	-105	3.3×10^{-8}	-101.2	6.0×10^{-8}	-97.8	7.2×10^{-8}	-95.5	9.4×10^{-8}	-92.5	9.8×10^{-8}
Al^{3+}	-119.7	4.4×10^{-8}	-116.1	6.9×10^{-8}	-115.8	5.2×10^{-8}	-110.3	5.8×10^{-8}	-109.6	8.73×10^{-8}	-109	1.1×10^{-7}	-107.4	1.2×10^{-7}
M.P.	-163.9	4.8×10^{-5}	-157.8	0.00025	-154.3	0.00021	-153.2	0.00116	-151.7	0.002494	-144.6	0.004034	-139.8	0.00474
P.P.	-166.5	6.6×10^{-5}	-161.2	0.00039	-160.7	0.00045	-159	0.00237	-155.3	0.003888	-153.2	0.011652	-150.4	0.01751
T.S.C.	-151.3	2.2×10^{-6}	-148.7	3.8×10^{-6}	-148.2	2.8×10^{-6}	-142.9	3.3×10^{-6}	-143.9	6.0×10^{-6}	-141.2	5.7×10^{-6}	-140.5	7.0×10^{-6}

Analysis of commercial tablets

In order to illustrate the technical use of the electrochemical sensor, two tablets for (ASP) were analyzed by MIP electrodes. The solutions was obtained by dissolving the specific

weight of commercial tablets in methanol solvent and diluted so that the tablet concentration range lies within calibration plot values. The DPVs value then was recorded under precisely the same conditions. The suggested technique was used to measure the concentration of all selected drugs in two types of pharmaceutical products. In order to verify the electro-chemical detection, we have compartmented the data results for parameters RSD%, RC% and Erel% with both detection methods including: direct potentiometric, standard addition method (SAM), multi standard addition method (MSA), by using ISE, as well as titration method and optimal chromatographic conditions. The results was indicated in (Table, 7&8)

Table (7). Recovery results and standard deviation of ASP-drugs obtained through the use of (MIP1+DBS).

Drug	Concentration Prepared/ M	Potentiometric methods	Concentration Found/ M	%Rec.	%RE	%RSD
Aspirin pure material	$1X10^{-3}$	Direct method	1.0312×10^{-3}	103.1	3.12	2.31
		SAM	1.0556×10^{-3}	103.22	3.22	2.07
		MSM	1.0402×10^{-3}	104.02	4.02	0.41
	$1X10^{-4}$	Direct method	1.0300×10^{-4}	103.15	3.15	1.55
		SAM	1.0455×10^{-4}	103.41	3.41	1.1
		MSM	1.0356×10^{-4}	103.56	3.56	0.22
Chewable tablet, acetylsalicylic acid (SDI)-IRAQ	$1X10^{-3}$	Direct method	1.0343×10^{-3}	103.42	3.42	0.92
		SAM	1.0554×10^{-3}	104.39	4.39	0.95
		MSM	1.0332×10^{-3}	103.32	3.32	0.33
	$1X10^{-4}$	Direct method	1.0279×10^{-4}	102.79	2.79	0.77
		SAM	1.0687×10^{-4}	104.57	4.57	2.2
		MSM	1.0310×10^{-4}	103.1	3.1	0.23
acidumacetylsaicylicum, Memphis/Bayer	$1X10^{-3}$	Direct method	1.0311×10^{-3}	103.12	3.11	1.4
		SAM	1.0541×10^{-3}	104.06	4.06	1.3
		MSM	1.0394×10^{-3}	103.94	3.94	0.26
	$1X10^{-4}$	Direct method	1.0315×10^{-4}	103.15	3.15	1.55
		SAM	1.0526×10^{-4}	103.74	3.74	1.68
		MSM	1.0353×10^{-4}	103.53	3.53	0.34

Table (8). Recovery results and standard deviation of ASP-drugs obtained through the use of (MIP2+DBS).

Drug	Concentration Prepared/ M	Potentiometric methods	Concentration Found/ M	%Rec.	%RE	%RSD
Aspirin pure material	$1X10^{-3}$	Direct method	1.0378×10^{-3}	103.78	3.78	1.71
		SAM	1.0528×10^{-3}	102.55	2.55	2.44
		MSM	1.0367×10^{-3}	103.67	3.67	0.48
	$1X10^{-4}$	Direct method	1.0370×10^{-4}	103.69	3.69	2.19
		SAM	1.0383×10^{-4}	102.42	2.42	1.79
		MSM	1.0260×10^{-4}	102.6	2.6	0.41
Chewable tablet, acetylsalicylic acid (SDI)-IRAQ	$1X10^{-3}$	Direct method	1.0451×10^{-3}	104.51	4.51	0.68
		SAM	1.0698×10^{-3}	104.2	4.2	2.44
		MSM	1.0323×10^{-3}	103.23	3.23	0.49
	$1X10^{-4}$	Direct method	1.0450×10^{-4}	104.53	4.53	1.51
		SAM	1.0498×10^{-4}	102.89	2.89	1.79
		MSM	1.0262×10^{-4}	102.62	2.62	0.41
acidumacetylsaicylicum, Memphis/Bayer	$1X10^{-3}$	Direct method	1.0456×10^{-3}	104.56	4.56	1.73
		SAM	1.0586×10^{-3}	103.77	3.77	2
		MSM	1.0376×10^{-3}	103.76	3.76	0.4
	$1X10^{-4}$	Direct method	1.0480×10^{-4}	104.81	4.81	1.92
		SAM	1.0626×10^{-4}	104.54	4.54	2.02
		MSM	1.0324×10^{-4}	103.24	3.24	0.47

Adsorption Isotherm

Adsorption isotherm is useful in understanding the adsorption mechanism of the adsorption template on a polymer surface. The collected data from the adsorption isotherm equilibrium were studied to illustrate the isotherm model Langmuir or Freundlich this was accomplished by plotting the ability of binding (Q) against free drug concentration, Q is determined according to the equation below: Adsorption isotherm produced after preparation of different concentrations of standard solution at room temperature is shown in (Figure,3). Experimental results for classifying experiments have been included in the (Table, 9).

Table (9). Rebinding values of (ASP) using [ASP –MIP_1] particles based on (VA).

Mass of MIP g	*[ASP-MIP_1(VA)]*			
	Ci mM	C_{free} mM	Q µMole /g	Q/C_{free} L/g
0.05	0.111	0.10866	0.4671	4.29825
	0.222	0.2181	0.7802	3.57724
	0.333	0.32494	1.6113	4.95868
0.1	0.111	0.10996	0.1043	0.94862
	0.222	0.21517	0.6834	3.17604
	0.333	0.31741	1.5592	4.91228

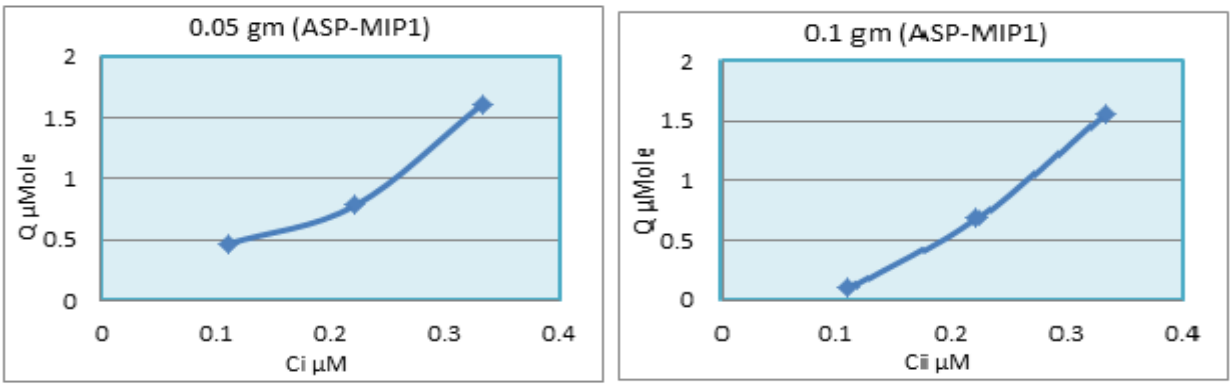


Figure (3): Binding isotherm of (ASP –MIP_1) using VA as monomers.

CONCLUSION

In this research, four electrodes were prepared based on MIP method using two monomer (VA, VIZ) and two different plasticizer (DBS, DOP), as it was observed that the interaction between template and the monomer was non-covently, therefore the ASP-drug was extracted easily to form selective cavity for estimation commercial ASP and excellent results obtained at lowest costs and with high accuracy.

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