SYNTHESIS, CHARACTERIZATION AND APPLICATION OF MEETHAMPHETAMINE – IMPRINTED POLYMERIC SOLID-PHASE

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ABSTRACT

This study was determine methamphetamine by the addition to the glycidyl methacrylate (GMA) monomer resulting from bulk polymerization formation. To acquire the highest adsorption capacity, molar ratios of the template, monomer, and cross-linking agent, as well as solvents and multiple monomers were investigated. Scanning Electron Microscopy (SEM) and Fourier Transform Infrared Spectroscopy (FTIR) were used to analyze the Methamphetamine polymer. The elution of Methamphetamine had a small effect on the surfaces of the three-dimensional network structure. Methamphetamine was successfully eluted using a mixture of methanol and acetic acid. The Methamphetamine adsorption capacities were 3.8145 and 9.01773 mol/g (Qmax), respectively. A Langmuir isotherm model follows Methamphetamine adsorption. Solid-phase extraction (SPE) syringes packed with molecular imprinted polymers (MIPs) were used to selectively separate and preconcentration the Methamphetamine from different patients.

Keywords: glycidyl methacrylate, monomers, crosslinker, isotherm

تحضير وتشخيص وتطبيق للاستخلاص المرحلة الصلبة البوليمرية المطبوعة للميثافيتامين والتركيز المسبق في مرضى مختلفين بواسطة اعمدة معبا

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المستخلص

يهدف البحث لتحديد الميثامفيتامين عن طريق اضافة مونمر كليسديل ميثاكريلايت الناتج من البامرة الصلدة للحصول على أعلى قدرة امتصاص ، تم فحص النسب المولية للقالب ، والمونومر ، وعامل الربط المتبادل ، وكذلك المذيبات Fourier Transform Infrared و (SEM) والمونومرات المتعددة. تم استخدام المسح المجهري الإلكتروني لتحليل بوليمر الميثامفيتامين. كان لشطف الميثامفيتامين تأثير ضئيل على أسطح بنية الشبكة Spectroscopy (FTIR) ثلاثية الأبعاد. تمت تصفية الميثامفيتامين بنجاح باستخدام خليط من الميثانول وحمض الخليك. كانت سعات امتصاص امتزاز Langmuir على التوالي. يتبع نموذج متساوي الحرارة (Qmax) الميتامفيتامين 3.8145 و 9.01773 مول / جم (MIPs) المليئة بالبوليمرات الجزيئية المطبوعة (SPE) الميثامفيتامين. تم استخدام محاقن الاستخراج ذات المرحلة الصلبة لفصل الميثامفيتامين بشكل انتقائي وتركيزه المسبق من مرضى مختلفين

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INTODUCTION

Methamphetamine (MAMP) is a drug that increases central nervous system activity. This drug affects euphoria and hallucinations and enhances the ability to stay awake (2, 3). Drugs that have strong promotional and addictive potential can cause a tolerance effect caused by toxic doses for their users (9, 11 13, 14). Because of the scarce information on the use of those drugs, the clinical and forensic laboratory routinely performs tests for MAMP and its metabolites (12, 18). Typically, samples can be processed in one of the following ways: solid phase extraction (SPE) and liquid phase extraction (LLE) (2-5). Initially, Molecular imprinted polymer MIP, the imprint molecule forms a complex of the actual monomers (1, 7, 16). After the polymerization cycle (10, 15, 19) as shown in figure (1), the functional groups are kept in place by a highly cross-linking polymer structure. In addition, the steric configuration of all these connections around with a given substratum and the template is really an important characteristic for formation of binding sites providing additional shape, size and flexibility to promote the selective identification followed by a high target affinity. As a result, the process of recognition in MIPs can be characterized in resemblance to enzyme-proven mechanisms – substratum-Complex is formed like the (lock/ key) model (7-10).

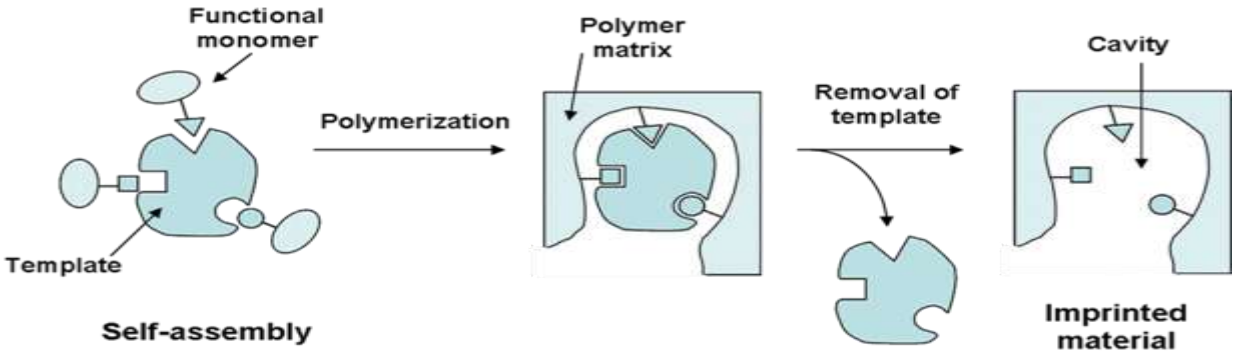


Figure 1. Molecular imprinted polymer cycle (8)

Certain MIP applications were prepared in SPE (12-15). The concentration of the solute in the fluid phase at a constant temperature provides an isotherm for absorption. Isotherms are the relationship between the concentrations of a solid and a liquid, and are used to describe the states of the absorption process (5). Solid phase extraction (SPE) is a technique designed for rapid selective sample preparation and then purification prior to chromatographic analysis methods (eg HPLC, GC, TLC). In SPE, after which one or more analytes are isolated by extraction from a liquid sample, partitioning, and/or adsorption to a solid stationary phase, Figure (2) (16).

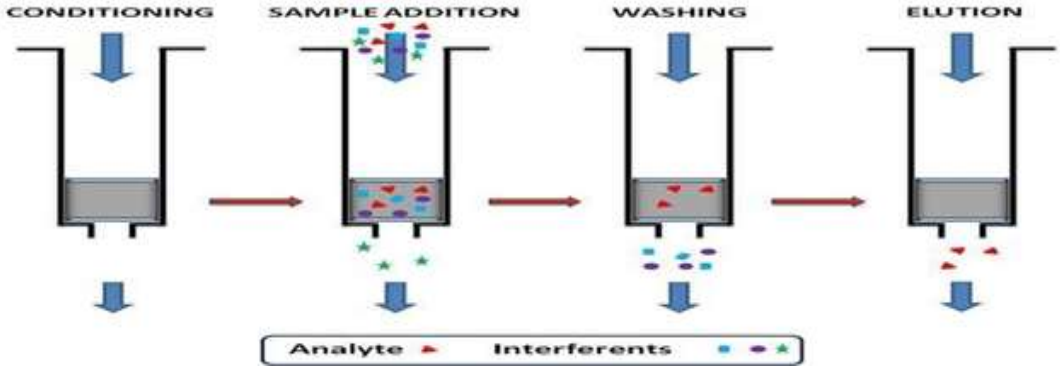


Figure 2. Illustrate the process of SPE

In this work identify The MIP preparation was performed in conjunction with the recognition cite glycidyl methacrylate with crosslinking allyl methacrylate, whereby benzoyl peroxide BPO functioned as the target molecule (methamphetamine) initiator. Subsequently, the impact of the monomer dosages on the adsorption performance was observed. The study also studied the adsorption behaviors with monomers bearing various functional groups and cross-linking agents, in addition to the percentage of solvents used. SEM, FTIR were used to characterize the prepared

MIPs. Furthermore, this research investigated the effect of solid phase extraction and initial methamphetamine concentration on adsorption capacity.

MATERIAIS AND METHODS

The source of the solvents used in the work as methanol, chloroform, acetonitrile and acetic acid from Merck (Darmstadt, Germany, www.merck.com).As for the basic materials, (glycidyl methacrylate) (GMA), (allyl methacrylate) (AMA) and benzoyl peroxide their source from Sigma–Aldrich (St. Louis, MO, USA, www.sigma-aldrich.com),Methamphetamine (MAMP) was provided from the medico legal institution (Baghdad, Iraq). nitrogen gas (99.99) from Arab gulf factory Baghdad.

MIP PROCEDURE

Preparation of Molecular imprinted polymer: For the preparation of the number one methamphetamine Molecular imprinted polymer (MAMP-MIP), Methamphetamine (0.6 g, 4 mmol) was dissolved in chloroform (10 mL), then mixed with glycidyl methacrylate (GMA) (2.27 g, 16 mmol) as a monomer in methanol (25 mL), and left for a few seconds at room temperature. Then, allyl methacrylate (AMA) (5.0 g, 40 mmol) was dissolved in methanol (50 mL) (as a cross-linker), and benzoyl peroxide (0.3 g) as an initiator) was dissolved in chloroform (5 mL) and added to the solution to obtain a homogeneous solution, and the mixture was shaken for 10 minutes. Afterwards, N2 gas was passed for 45 minutes through the mixture to extract oxygen from it. The solution was then placed in a water bath at 60 °C for 12 hours. When the reaction was completed and the MAMP-MIP was formed as very hard materials, they were left for 24 hours to dry, and then they were crushed and ground by a mortar and pestle. A sieve was used to obtain particles with a diameter of 125 μm which were then collected. methamphetamine was extracted from polymers MAMP-MIP using a soxhlet of (60:10:30, v/v/v) acetonitrile/acetic acid/doubly-distilled water for weak extraction. After ensuring complete template removal, the polymer was dried for 24 hours at room temperature and collected to be used as a substance in a solid-phase extraction syringe. Each plastic syringe (column) was packed with MAMP-MIP (250 mg) and used a 3 mL solution for solid-phase extraction by a peristaltic pump.

SAMPLING PROCEDURE

Serial concentrations (30, 60, 90, 120, 150 ppm) of methamphetamine were prepared and passed through the column at a flow rate of 70 rpm. The extraction column was washed twice with 2 mL of distilled water to remove substrate interference and then the MIP was removed. The device consisted of a 3 mL plastic syringe filled with (0.2, 0.4 g) filled with pre-crushed and sieved MIP with a bore size of (125) μm. Methamphetamine urine samples were collected and centrifuged at 5000 rpm for 15 min to remove any sediment. Unmodified and saturated methamphetamine was extracted by a vertical column.

PROCEDURE OF EXTRACTION METHOD

Different urine samples were extracted depending on the methamphetamine-prepared column filled with MIP (0.2, 0.4 g), reservoir volume, 3 ml. The SPE blank was loaded with the supernatant from the urine sample by centrifugation at a flow rate of (70 mL min-1), (60:10:30, vol/vol/vol) acetonitrile/acetic acid/double distilled water added to a collection column and rinsed after rinsing in small beaker. Then dry for 10 minutes. 1 ml acetic acid/acetonitrile (1:100, vol/vol) was added and water was also collected in the same baker and the residue was dried again in a water bath at 50 °C.

RESULTS AND DISCUSSION

After passing the solution of methamphetamine in syringe packed with MAMP-MIP the residue which has less absorption was measured by UV-VIS that indicate to lower concentration at final process, for good expressive example of the advantages of the use of impressed polymers in SPE in the quantification of the methamphetamine show figure (3).

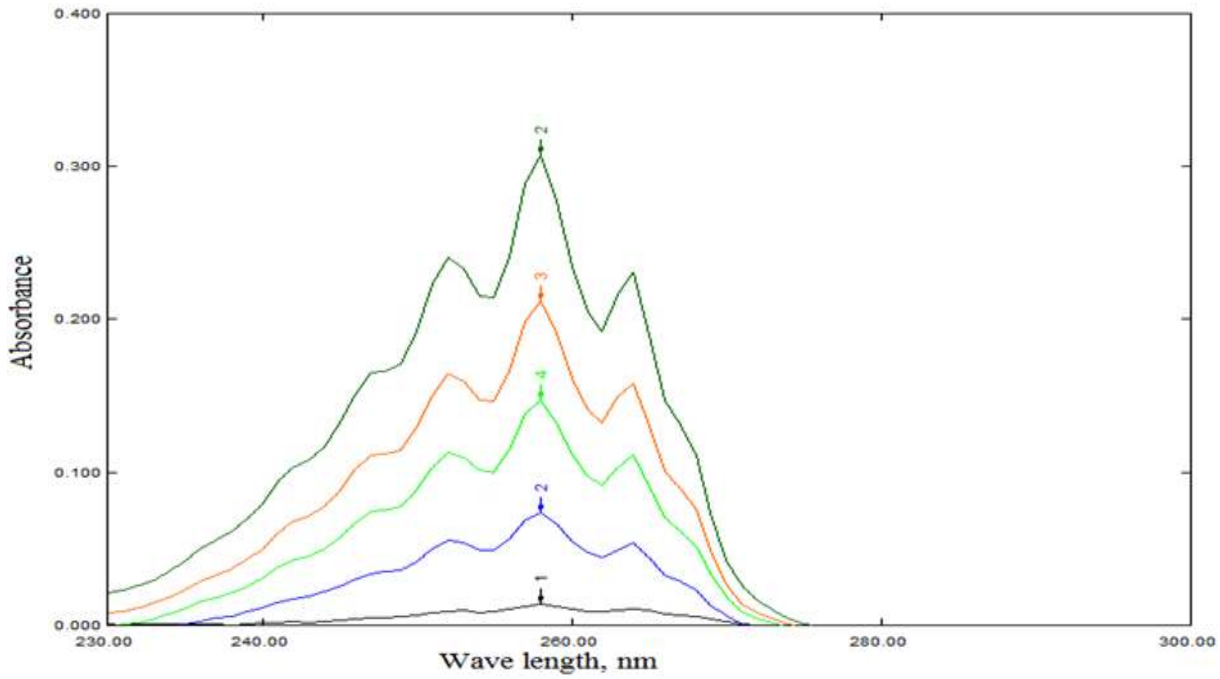


Figure 3. The absorption at 258 nm of the concentration of Methamphetamine standard at (15, 20, 25, 30 and 35) ppm respectively

FTIR of molecularly imprinted polymers for (MAMP): The functional groups present in a compound can be detected using a FTIR Fourier transmission infrared spectrometer, which comprises a significant chemical characterization process. The methamphetamine FTIR spectra presents multiple functional groups, in addition to MAMP-MIP both prior to and following the methamphetamine template removal (see Figures (4 ,5, 6) for MAMP-MIP.

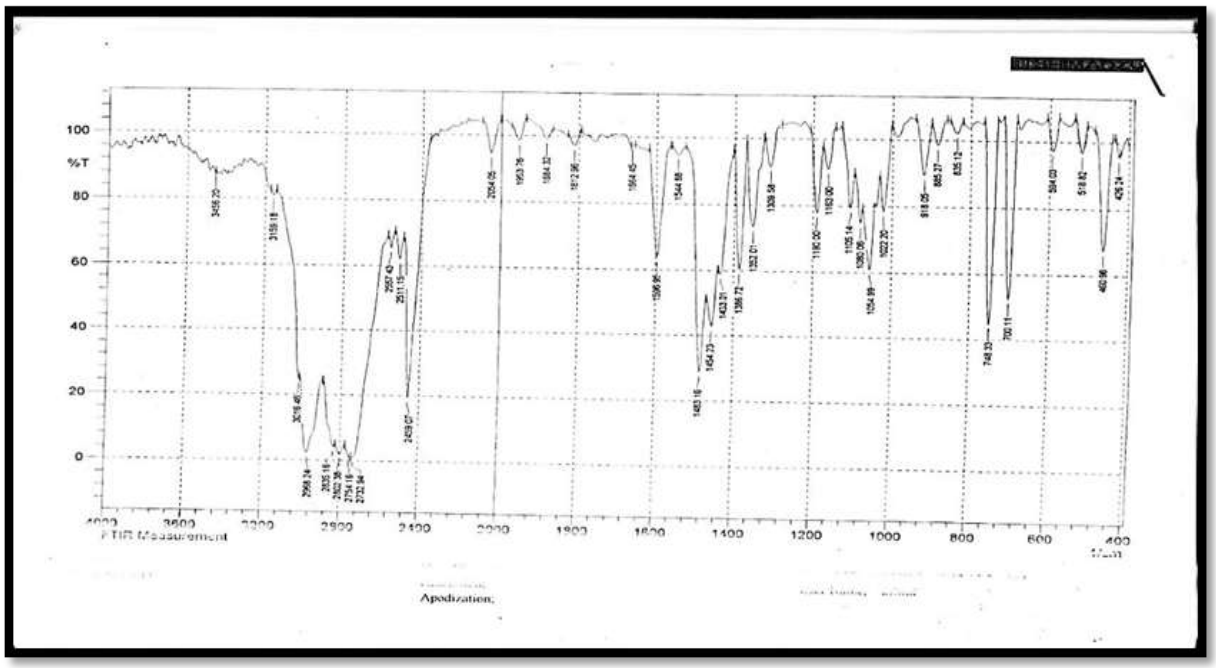


Figure 4. FTIR spectrum of standard MAMP

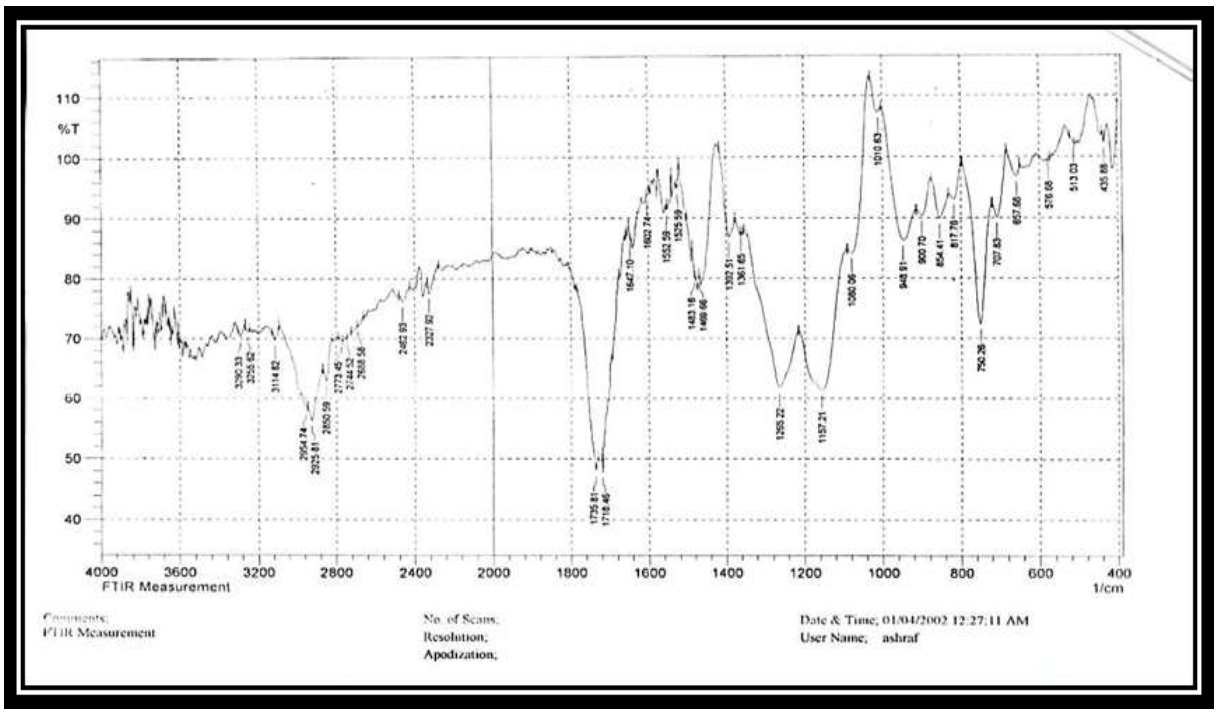


Figure 5. the FTIR spectrum of MAMP-MIP(GMA) before the abstraction of (MAMP)

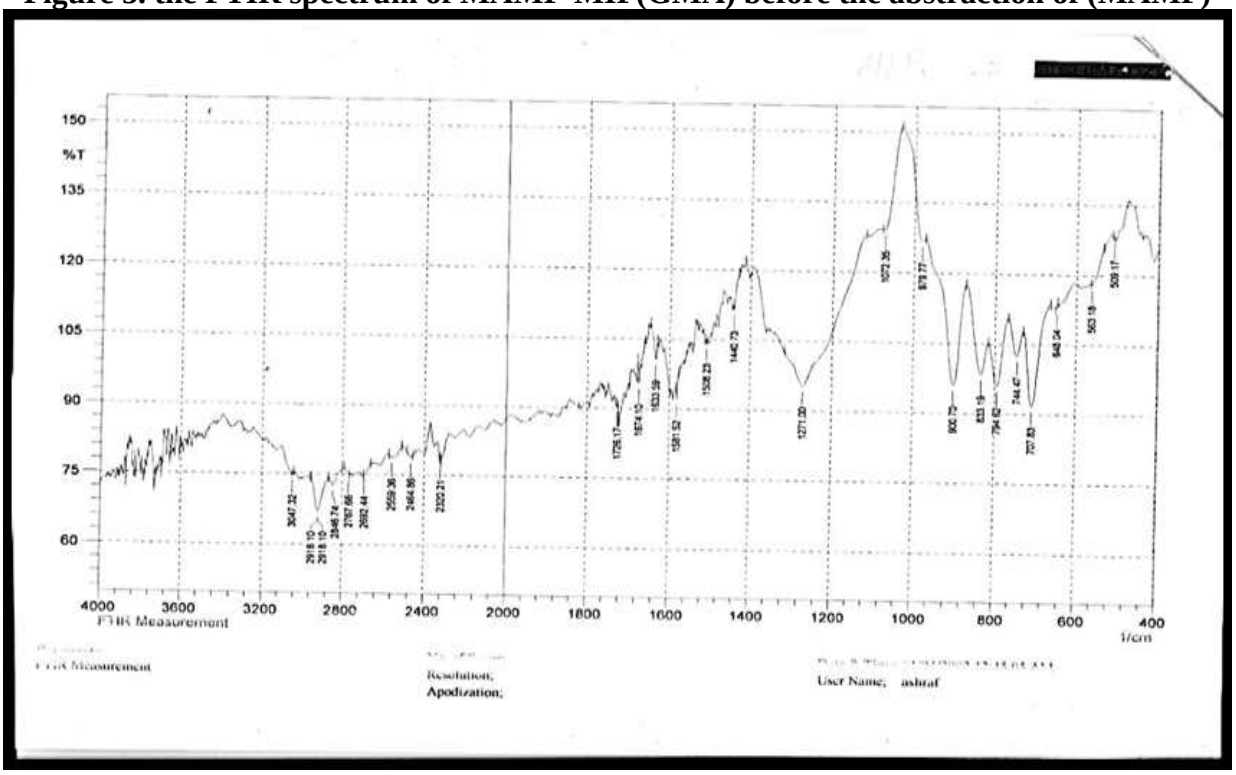


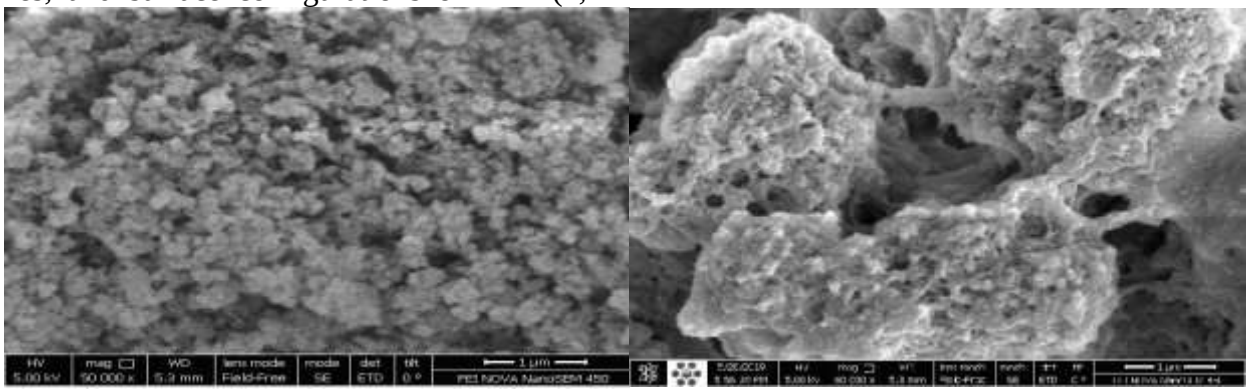
Figure 6. the FTIR spectrum of MAMP-MIP(GMA) after the abstraction of (MAMP)

The instantaneous transmission infrared spectrophotometry spectra of imprinted methamphetamine (MAMP) and the polymer MAMP-MIP was recorded in the range of 400–4000 cm-1 used KBr pellet method (Table 1). the table show FTIR spectrum of MAMP following bands: (3456, 3016, 1596, 1483, 748 and 700) cm-1 for N-H, C-H, C-H aromatic expansion. C − H bending and off-plan bending of the substituted monomer. The FTIR spectrum of MAMP-MIP (MTAA) before demoulding showed the following bands (3269, 3074, 1776, 1631, 1587, 1149, 802, 746) cm-1 for N–H expansion, aromatic C–H Stretching, Carbonyl acid stretching, C = C stretching, C–O–C stretching, and out-of-chart bending of the substituted monomeric ring. Show the FTIR spectrum of MAMP-MIP(GMA) after the abstraction of (MAMP) disappearance C=C stretching, N–H stretching and an out-of-pattern curvature of the single substituted ring superimposed in the template

(MAMP) spectrum indicating drug extraction from the template. When using acrylamide (AAM) as a monomer for the synthesis of another methamphetamine (MAMP) MIP.

Scanning electron microscopy SEM

The morphological evaluation is critical to the appreciation of the morphological traits, cavity sizes, and surface configurations of MIP (4, 17) both prior to and following the methamphetamine template removal. SEM images were used to analyse the morphology of the MAMP-MIP. Figure 9 (A,B) show the surface morphologies of the particles and cavities before and after elution for methamphetamine.



A **B**

Figure 7 - SEM surface geometry of MAMP-MIP, (A) before methamphetamine abstraction, (B) after methamphetamine abstraction

Several studies have been performed using different ratios (D:M:C) to arrive at the most accurate ratio of MIP preparation (MAMP). Among these studies of the (D:M:C) ratios of (1.5:3.5:17.5) for MAMP-MIP yielded a list of suitable properties for the polymer in Table 1.

Table 1 Molarity ratios of [D:M:C] and the ratios used in the preparation of MAMP-MIP

		Drug MAMP	Monomer Glycidyl methacrylate	Cross linker allyl methacrylate	Initiator Benzoyl peroxide	Solvent	Result
MIP	%	4.761	19.047	76.190	0.3	10 mL	Pale
	Mmole	1.00	4.00	16.00	0.32	CHCl3	white
MIP	%	7.407	18.518	74.074	0.3	10 mL	Pale
	Mmole	2.00	5.00	20.00	0.32	CHCl3	white
MIP	%	6.666	15.555	77.777	0.3	10 mL	Pale
	Mmole	1.50	3.50	17.50	0.32	CHCl3	white

Adsorption capacity and pre-concentration

A series of absorption achievement for different initial concentrations of MAMP – MIP ranging from 0.07 to 0.9 µmol/ml on adsorption capacity µmol/g was studied using the following equation (6):

$$\mathbf{Q} = (\boldsymbol{Ci} - \boldsymbol{Cf})\left(\frac{\mu\mathbf{mol}}{\mathbf{ml}}\right) * \frac{\boldsymbol{vol}\ (\boldsymbol{ml})}{\boldsymbol{Wof\ Mip(g)}}$$

The concentrations from (0.1281-0.6862) µmol/ml consume 3ml range of volumes, when using 0.1g weight of MAMP-MIP show in table 2.

Table 2. The optimal synthesis conditions for the molecularly imprinted polymer for methamphetamine

W/ MIP (g)	Ci (ppm)	Cf (µmol/ml)	Q µMole /g	Q/Cfree L/g	Vol (ml)
0.1	0.2010	0.1281	4.374	34.145	6
	0.4020	0.2572	8.688	33.779	6
	0.6030	0.5360	4.02	7.5	6
	0.8040	0.6729	7.866	11.6897	6
	1.005	0.6862	19.128	27.875	6

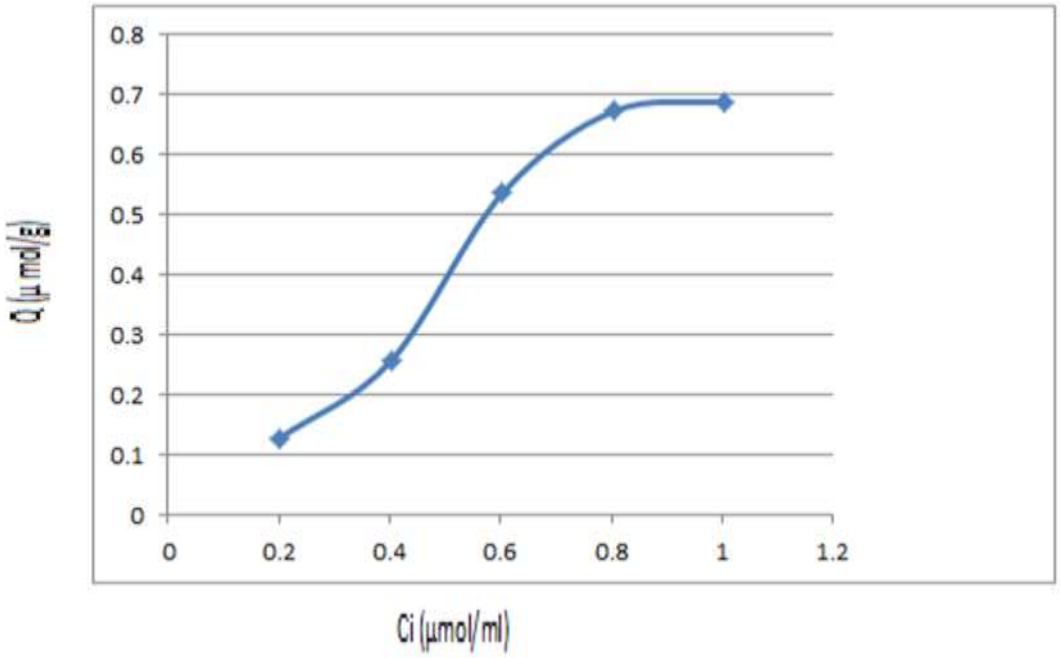


Figure 8. The relation between initial concentration Ci (µmol/ml) and capacity Q (µmol/g)

From figure 8 the Langmuir type was chosen because the findings demonstrated that the concentration rises proportionately to the rise in absorbance, yielding one slope

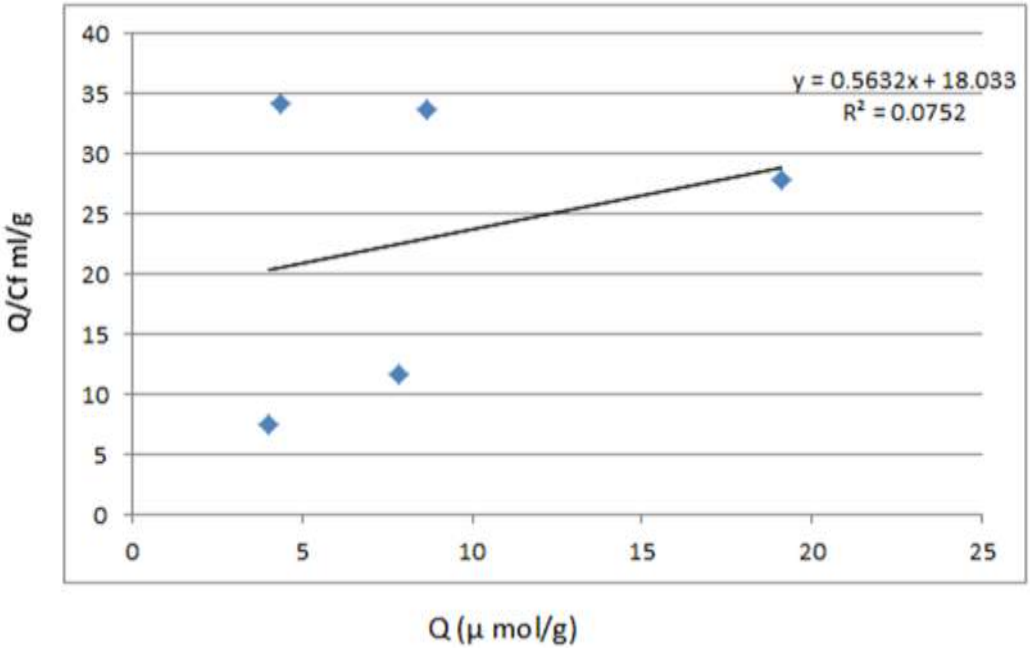


Figure 9.The relation between capacity Q (µmol/g) and Q/Cf (mL/g)

Slop = -1/kd

0.5632 = -1/ kd =1.775

Intercept = Q_{max}/kd

18.033 = Q_{max}/1.775

Q_{max} = 32.008µmol/g

Urine samples analysis

Under optimal conditions, MAMP-MIP was applied homogeneously to determine methamphetamine in urine samples. It was a matrix, first-step urine sample and step-by-step, post-extraction procedure. Unity in the gradient can be achieved by flowing through the plastic syringe into the peristaltic pump. It is expected that it will be emitted from re-editing again. By extending the wash time from 125 seconds to 5 minutes, matrix peaks were visibly suppressed. This can be demonstrated with a 3-minute sample spray of a laundry aerosol. A version of this example is obtained from satisfactory methamphetamine results: a sample containing 0.1 gram of MAMP-MIP was taken and the results were show in the table (3).

Table 3. Standard addition method for drug determination using imprinted polymer method solid phase extraction used MAMP-MIP

Wt. of MIP (g)	Conc. of solution (ppm)	Synthetic solution Conc. Taken (ppm)	Synthetic solution Conc. Found (ppm)	% Recovery	No. of Patients	Drug conc. (ppm)	% Recovery	RSD%
0.1	30	30	29.86	99.53	1	27.97	93.23	3.65
					2	29.62	98.87	1.72
					3	26.95	89.83	1.95
					4	28.21	94.03	2.55
					5	28.24	94.53	1.93
0.1	60	60	59.53	99.21	1	58.56	97.60	2.73
					2	59.36	98.93	1.29
					3	58.72	97.86	1.84
					4	57.94	96.56	2.93
					5	57.82	96.36	2.97
0.2	30	30	29.62	98.73	1	27.96	93.20	1.84
					2	28.32	94.40	2.41
					3	28.37	94.56	1.72
					4	29.61	98.70	2.29
					5	28.84	96.13	2.11
0.2	60	60	59.77	99.61	1	58.95	98.25	2.33
					2	59.29	98.81	1.52
					3	58.82	98.03	1.59
					4	59.38	98.96	1.74
					5	59.41	99.01	2.66

Average of three measurements

The values in Table 3 reflect the MIP method used to detect methamphetamine and estimated to be using GC-Mass. The results obtained were for methamphetamine and its derivatives as found in the applied figures, as shown in Figures 10 and 11.

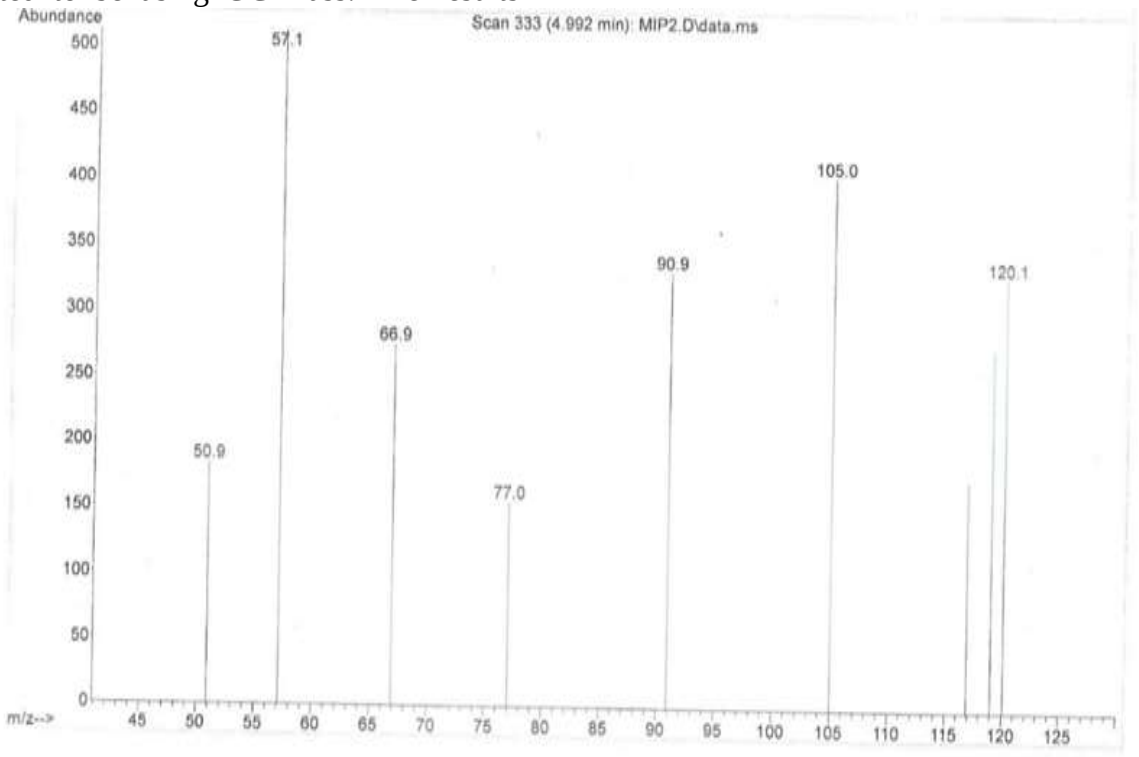


Figure 10. GC/MS structure of methamphetamine derivatives (4- Ethylphenethylamine) after extracted used MIP-MAMP

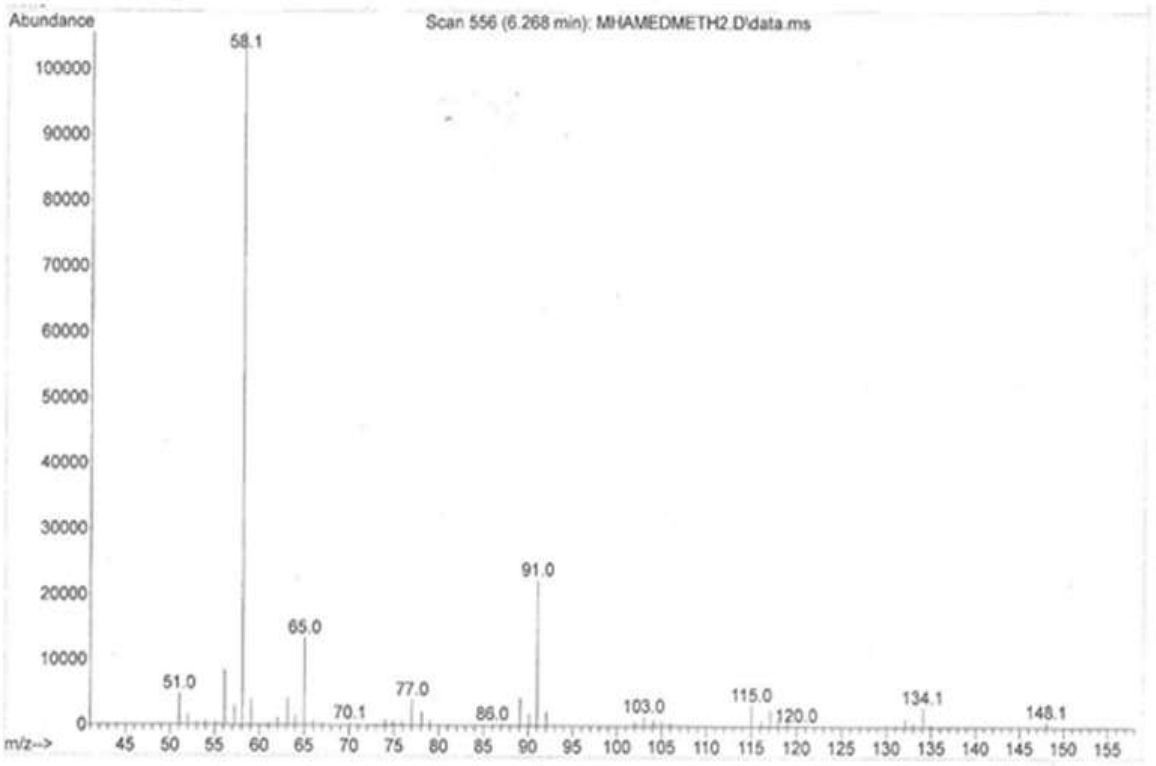


Figure 11. GC/MS chromatogram for the amphetamine after extracted used MIP-MAMP

CONCUSION

In this research, chemical sensors were prepared based on the quality of the preparation and on monomers of different aggregates using a crosslinker to give the appropriate geometric shapes to obtain molecularly imprinted polymers (MIP), and from these shapes the capacity required to print a drug can be studied. In this way, the drug was estimated at very low. concentrations and in different mixtures. The preparation steps of molecularly imprinted methamphetamine polymers include the following: first is the preparation of molecular imprinting and the second is to obtain a low dose of drug for the concentration process using solid-state extraction, thus obtaining a concentration and quantification process in one step.

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