ESTIMATION TRACE OF HEROIN EXTRACTED FROM TOXIC PLANTS USING MOLECULARLY PRECIPITATION POLYMERS TECHNOLOGY

Y. K. Al-Bayati[1] N. R. Jber[2] S. F. Abdullah[3]
Prof. Prof. Assist. Lecturer
Dept. of Chem., Coll. of Sci., University of Baghdad
Dept. of Chem., Coll. of Sc., Al-Nahrain University, Baghdad
Coll. of dentistry, Al_Iraqia University
Email:yehya.kamal@sc.uobaghdad.edu.iq

ABSTRACT

This study aimed to investigate the specific adsorption of heroin made from morphine that extracted opium. Using acrylamide and n-iso propyiacrylamide as the functional monomers, n,n′-methylenebisacrylamide as the crosslinker, and benzoyl peroxide as the initiator. At bulk heroin concentrations of 20, 40, 60, 80, and 100 ppm in ethanol solution, this MIP's maximum heroin adsorption capacity of 3.87 mg/g at used 0.2 gm acrylamide as monomer which was among the best capacities documented in the literature to date. The adsorption capacity, selectivity separation, reusability, and chemical stabilities of the molecularly imprinted polymers were confirmed by thermodynamic analysis, experimental characterization, adsorption investigations, and recommended protocols. FTIR, UV-vis, and scanning electron microscopy were used to observe the analytes. Three measurements taken during two patient repeat tests at 20–100 ppm of heroin have relative standard deviations (RSD%) ranging from 1.94% to 4.27%. In human urine samples that were tampered with, the relative recoveries for heroin range from 92.5 to 103.75%.

Keywords: Analysis of toxicological effects; solid phase extraction of dangerous plants

تقدير أثر الهيروين المستخرج من النباتات السامة باستخدام تكنولوجيا البوليمرات الترسيبية الجزيئية

يحيى كمال البياتي[1] نسرين رحيم جبر[2] سجى فرحان عبدالله[3]
استاذ استاذ مدرس مساعد
قسم الكيمياء، كلية العلوم، جامعة بغداد قسم الكيمياء، كلية العلوم، جامعة النهرين كلية طب الأسنان، الجامعة العراقية

المستخلص

البحث يهدف الى تحديد الهيروين المصنوع من المورفين المستخرج من الأفيون عن طريق استخدام تقنية بلمرة الترسيب لإنشاء بوليمرات مطبوعة جزيئيًا .باستخدام بيروكسيد البنزويل كبادئ، و ن،ن–مثيلين بساكريل اميد كرابط متشابك، و اكريل اميد ون– ايزوبروبيل اكريل اميد كمونومرات وظيفية. أظهر هذا الطبعات أقصى قدرة لامتصاص المورفين تبلغ 3.87 ملغم/غم ضمن تراكيز من الهيروين يبلغ (20،40،60،80،100) جزء في المليون في محلول الايثانول، وهي واحدة من أعظم ما تم تسجيله حتى الآن. أثبت التحليل الديناميكي الحراري، والتوصيف الآلي، ودراسات الامتزاز، والآليات المقترحة قدرة امتزاز الطبعات المحضرة، والانتقائية، وقابلية إعادة الاستخدام، والثبات الميكانيكي والكيميائي. تم استخدام اطياف الاشعة تحت الحمراء، والأشعة فوق البنفسجية، والمجهر الإلكتروني الماسح لمراقبة التحاليل. ثلاثة قياسات تم إجراؤها أثناء اختبارين متكررين للمريض عند 20–100 جزء في المليون من الهيروين لها انحرافات معيارية نسبية (RSD٪) تتراوح من 1.94٪ إلى 4.27٪. في عينات البول البشري التي تم العبث بها، تتراوح نسب الاسترداد النسبي للهيروين من 92.5 إلى 103.75٪.

الكلمات المفتاحية: تحليل التأثيرات السمية؛ استخلاص الطور الصلب للنباتات الخطرة

Received: 27/1/2025, Accepted:23/4/2025, Published: August,2025

INTRODUCTION

The medical prescription of high dosages of pharmaceutically pure heroin (diacetylmorphine) to patients who are otherwise resistant to therapy for heroin addiction is gaining attention on a global scale (13). In studies conducted in Switzerland and the Netherlands, heroin-assisted treatment has significantly improved patients' physical, mental, and social well-being as well as their surroundings (16, 27, 28). Canada and many other European countries are conducting clinical trials in which heroin is administered to. Heroin is derived from lipophilic, semi-synthetic morphine (6, 17, 18). The phenanthrene ring's 3- and 6-carbon sites are joined by two acetyl groups (Fig. 1). (14-18). Lastly, the liver, along with most likely the kidney and brain, produces the morphine-3-glucuronide (M3G) and morphine-6-glucuronide (M6G) conjugates . Heroin's pharmacodynamic activity lasts for several hours, despite its extremely short estimated half-life of two to five minutes (10). Its more stable agonistic metabolites, 6-monoacetylmorphine, morphine, and morphine-6-glucuronide, are primarily responsible for its action (5). Therefore, we expanded our bioanalytical technique to include the measurement of methadone and its metabolite ethyl-5-methyl-3,3-diphenyl-1-pyrroline (EMDP) in plasma in order to investigate potential interactions between the two opioids. Under the close supervision of a nursing staff, heroin is administered at outpatient clinics (7, 8). Opium poppies are used to make heroin, and the usage of illegal heroin in addition to pharmaceutical-grade heroin can be identified by looking for opium derivative impurities (2, 3, 20). Morphine similar to other addictive drugs in human plasma can all be analyzed using gas chromatographic (GC) techniques (1,15). Derivatization of the analytes is required for GC analysis, a laborious procedure that may cause further heroin hydrolysis. In human plasma and mouse serum several HPLC approaches are also described for the detection of the long-circulating heroin metabolites without actually detecting the pro-drug heroin and its metabolite (4). Both morphine and its glucuronides. 6. Acetylmorphine (10-11). However, the recovery of heroin and its metabolites in human plasma was only 44.8–66.8% in these trials, which used automated sample preparation on C18 columns at ambient temperature (21). The measurement of heroin was hampered by endogenous substances when diode array detection was used. MS/MS was used in our investigation to improve the detection's sensitivity and specificity (22, 23). To put it briefly, our goal was to create a quantitative test for heroin, methadone, and their metabolites that could also identify any cocaine and illegal heroin use in individuals receiving treatment for heroin. We present an LC-MS/MS assay that met our specifications (19). The stability of the analytes was given particular consideration during sample pre-treatment. The experimental results indicate that the MIP-SPE sensor has the following advantages ,it is more stable, highly sensitive and selective, doesn't need prior labeling, and is very easy to use. The previously suggested techniques only require small amounts of polymer and would also be effective for expensive target molecules like poisons.

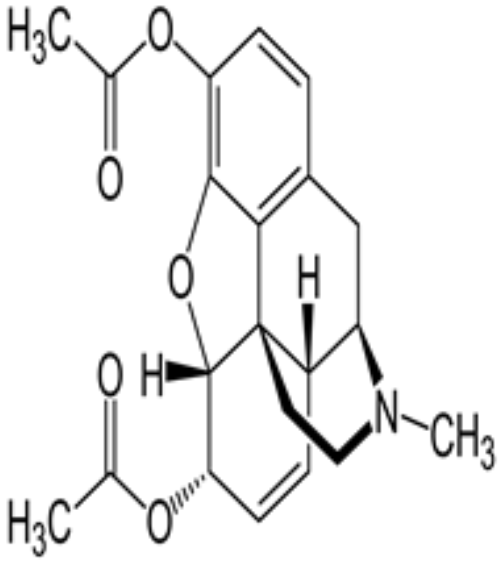


Fig 1. Chemical structure of heroin

MATERIALS AND METHODS

The heroin was provided by the medicolegal institute in Baghdad, Iraq. Benzoyl peroxide (BPO) ,Acrylamide (AAM), n-iso propyiacrylamide (NIPAA), and n,n′-methylenebisacrylamide (NNMBA), were supplied by Sigma–Aldrich (St. Louis, MO, USA, www.sigma-aldrich.com), while ethanol, chloroform, and acetic acid were supplied by Merck (Darmstadt, Germany,

www.merck.com). 99.98 nitrogen gas from the Baghdad-based Arab Gulf facility.

INSTRUMENTATION

A Shimadzu UV spectrophotometer 1800 PC and a JSM.6390A scanning electron microscope were used for the control. Heating and series FTIR Shimadzu (FTIR)-8000 (Japan). After being pre-washed, MIP-opioid uptake was evaluated once again under UV light to make sure all of the heroin had been eliminated. With a wavelength of 230 nm, pure heroin was first tested for consumption using this method. To stir the prepolymer solution, Sonerx (W. Germany) was utilized.

MIP PROCEDURE

For TLC analysis of opium alkaloids from Papaver plants, a solid-phase extraction technique that is both quick and accurate was developed. Five milliliters of 5% acetic acid were used to sonicate fifty milligrams of dried and powdered plant material for thirty minutes. Following centrifugation, 3 milliliters of the supernatant were put onto a paper TLC solid-phase extraction cartridge and washed with 0.1 M methanol and hydrochloric acid.Based on the retardation factor, morphine was isolated from the other substances (codeine, oripavine, thebaine, papaverine, noscapine, and sanguinarine). After sublimating the morphine in 5 milliliters of anhydrous acetic acid for two hours at 85 degrees Celsius, the solution was cooled, and heroin precipitated out of the mixture. After 1 mmol (0.369 g) of the template (heroin) was dissolved in 2 ml of a porogen solvent (1:9) ethanol:acetonitrile, 4 mmol (0.284 gm) of acrylamide and 2 mmol (0.226 g) of n-isopropyiacrylamide were added, respectively. Then, using ultrasonography, the liquid was agitated for ten minutes. For each, 0.33 mg of initiator (benzoyl peroxide) and 12 mmol (1.850 gm) of cross linker (n,n′-methylenebisacrylamide) were added. After passing N2 gas through the prepolymerization stage solution for 25 minutes, the stopper sealed the tube. After that, the tubs spent 12 hours in the water bath at 60°C. The polymerization processes were completed during that period, and heroin-MIPs were produced. Following the removal of the template and the removal of all non-reacted compounds from the MIP combination in the soxhlet, the mixture was cleaned using an excess of ethanol/acetic acid (9:1, v/v) solvent. After that, the results were vacuum-dried for four hours (5-8).

The synthetic MIP was made and then dried for an hour at thirty degrees in a drying oven. Next, use a mortar and pestle to smash and grind the mixture until the particles are 125 µm in size. utilized as extraction needles prior to the sampling equipment being extracted. A plastic syringe was used to insert the prepared (MIP) into the plastic syringe (Column). Poured from the top of the column, the solution—either urine or a standard solution moved at a speed of 75 revolutions per minute because of suction (23).

SAMPLING

Create a stock solution with 20, 40, 60, 80, and 100 parts per million of heroin at pH 6.8, then run it through a column at 100 revolutions per minute. To eliminate any matrix interference, the column was cleaned three times using four milliliters of distilled water after being taken out of the MIP. Different weights (0.2 and 0.4 g) of MIP that had been previously ground and sieved (125 microns) were placed in each 3 ml plastic syringe (6).

Real sampling

Urine samples that most likely included morphine were ordered to be transferred to Baghdad, Iraq, for forensic analysis by the judge. The centrifuge sample was spun for five minutes at 5,000 rpm to remove any precipitation. Following the removal of the squid and non-pointed samples using a column, the heroin was immediately added to the urine supernatant.

Extraction procedure

Heroin was extracted from the urine using a MIP heroin solid phase extraction (SPE) column. A 3 ml plastic syringe was initially filled with 0.2 g of MIP in order to make this column. At a flow rate of 45 rpm, the supernatant from the urine sample that had been centrifuged was put into the space above the SPE column packing. The eluent was collected in a small beaker following the addition of nine milliliter of ethanol to the distilled water, one milliliter of acetonitrile, and four percent acetic acid to the column. The residue was dried in a water bath set at fifty degrees Celsius for 15 minutes and then again.

One milliliter of residue remained after the combination had reached room temperature, and a jet of nitrogen had completely evaporated the solvent (24).

RESULTS AND DISCUSSION

Synthesis of MIPs for heroin : Two heroin MIPs were implanted utilizing a non-covalent bulk polymerization method known as self-assembly. Functional monomers have shown great promise in studying template interactions. Acrylamide and n-isopropyiacrylamide were the two monomers used.

FTIR analysis

The use of FTIR to determine the functional groups present in a molecule is an essential step in the chemical characterization process. Table 1 shows the various MIPs' FTIR spectra.

Table 1. Using acrylamide as a functional monomer, the heroin-imprinted polymer's most prominent peaks in the FT-IR spectra

Functional Group cm^{-1}	Heroin	Heroin –MIP acrylamide before heroin removal	Heroin -MIP acrylamide after heroin removal
C=O ester.	1735	1733	_____
CH-aliphatic.	2954, 2862	2975, 2852	2966, 2844
Ar-H.	3072	3068	_____
C=C aromatic.	1598	1602	_____
C=C aliphatic.	1612	1624	1621
C-O .str.	1245	1234	_____
$C=CH_2$ str.	_____	1622	1621
C=O amide.	_____	1685	1688
$N-H_2$, N-H str.	_____	3452, 3361, 3281	3460 , 3370, 3238

The infrared Fourier transmission spectra of heroin-imprinted polymers, MIP, both leached and unleached, in the 400–4000 cm-1 range were recorded using the KBr pellet technique. According to Table 1, the heroin's FTIR spectra displayed the following bands: 1735, 2954 and 2862, 3072, 1598, 1612, and 1245. C=O ester, C-H aliphatic, Ar-H, C=C aromatic, C=C aliphatic, C-O, C=CH2, C=O amide, and N-H2 are all described by the values of cm-1. The following bands are seen in the heroin-MIP (acrylamide) FTIR spectra prior to the template being eliminated. Consequently, the lengths of the stretching C=O ester, C-H aliphatic, Ar-H, C=C aromatic, C=C aliph. and C-O str. are (1733 , 2975 and 2852 , 3068 , 1602 , 1624 , and 1234) cm^{-1}. Consequently, N-H2, C=CH2, C=O amide, and N-H str have lengths of (1622, 1685 , 3452 , 3361 , and 3281) cm^{-1}, respectively. The drug has been extracted from the template if the MIP (acrylamide) FTIR spectrum after template removal shows no evidence of C=O ester, Ar-H, C=C aromatic, or C-O stretching that excises in the template (heroin) spectrum. When n-iso propyiacrylamide is utilized as the monomer for the synthesis of additional MIPs for morphine consumption, The MIPs' FTIR spectra are displayed in Table 2 both before to and following template removal.

Table 2. FT-IR spectra of heroin-imprinted polymers employing n-iso propyiacrylamide as a functional monomer show the most prominent peaks

Functional Group cm^{-1}	Heroin	Heroin -MIP n-iso propyiacrylamide before heroin removal	Heroin -MIP n-iso propyiacrylamide after heroin removal
C=O ester.	1735	1737	_____
CH-aliphatic.	2954, 2862	2956,2837	2991,2958
Ar-H.	3072	3061	_____
C=C aromatic.	1598	1604	_____
C=C aliphatic.	1612	1618	1623
C-O .str.	1245	1248	_____
$C=CH_2$.	_____	1627	1624
C=O amide.	_____	1687	1691
N-H str.	_____	3371	3368

The heroin's FTIR spectra, which were extracted from Tables (3,6), showed the following bands. (1735, 2954 and 2862, 3072, 1598, 1612, and 1245)cm^{-1}. C=O ester, C-H aliphatic, Ar-H, C=C aromatic, C=C aliphatic, C-O, C=CH2, C=O amide, and N-H str is

described by a cm^{-1} value. The following bands are visible in the heroin-MIP (n-iso propyiacrylamide) FTIR spectra prior to the template being removed. The(1737, 2956 and 2837, 3061, 1604, 1618, and 1248) cm^{-1} are the lengths of Ar-H, C=C aromatic, C=C aliphatic, C=O ester, C-H aliphatic, and C-O stretching, respectively. C=CH2, C=O amide, and N-H str have respective lengths of (1627 , 1685 , and 3371) cm^{-1}. Once the template is removed, the MIP (n-iso propyiacrylamide) FTIR spectrum shows that the drug has been extracted from it because the template (heroin) spectra no longer exhibit any C=O ester stretching, AR-H stretching, C=C aromatic, or C-O stretching. To find the ideal ratio for the synthesis of MIPs (heroin), numerous tests with various ratios (D: M: C) were conducted. These studies, which use the heroin-MIP molar ratios (D: M: C) of 5.882: 23.529:70.588 and 5.882:11.764:82.352, have generated a list of polymers with the required characteristics. In Table 3, this list is shown.

Table 3. The ratios of [D:M:C] and progeny variation used in the production of heroin MIPs

		Drug Heroin	Monomer acrylamide	Cross linker n,n′-methylenebis acrylamide	Solvent	Result
MIP1	%	5.882	35.294	58.823	10ml C_2H_5OH	White
	mm	1.00	6.00	10.00		
MIP2	%	55.555	16.666	77.777	10ml C_2H_5OH	White
	Mm	1.00	3.00	14.00		
MIP3	%	5.263	21.052	73.684	10ml C_2H_5OH	Yellow
	mm	1.00	4.00	14.00		
MIP4	%	5.882	23.529	70.588	10ml C_2H_5OH	White
	Mm	1.00	4.00	12.00		
		Drug Heroin	**Monomer n-iso propyiacrylamide**	**Cross linker n,n′-methylenebis acrylamide**	**Solvent**	**Result**
MIP1	%	5.882	23.529	70.588	10ml C_2H_5OH	White
	mm	1.00	4.00	12.00		
MIP2	%	5.263	21.052	73.684	10ml C_2H_5OH	yellow
	mm	1.00	4.00	14.00		
MIP3	%	7.692	15.384	76.923	10ml C_2H_5OH	Yellow
	mm	1.00	2.00	10.00		
MIP4	%	5.882	11.764	82.352	10ml C_2H_5OH	White
	Mm	1.00	2.00	14.00		

Number of samples: (n=2) and the number of repetitions(n=5) times for each MIP synthesis

In the 400–4000 cm-1 range, The Fourier transmission infrared spectrometry spectra of leached and unleached heroin imprinted polymers were recorded using the KBr pellet technique, or MIP, in combination with a Soxhlet extraction procedure can effectively remove the template molecule from the polymer framework.

Adsorption isotherm : With the help of isotherm adsorption, Perhaps a better understanding of it is feasible to use the adsorption mechanism of the adsorption template with a polymer surface. The equilibrium of isotherm adsorption data was assessed in order to identify the kind of isotherm Langmuir or Freundlich models. The drug's bind-ability (Q) was plotted in order to

make this judgment, which is calculated using the following formula, against its free concentration.

Q = [(Ci – Cf) Vs *1000] / MMIP……1

Ci , Cf, (µmol / mL) , Vs (mL), and MMIP(mg) initial and final drug concentration , volume , mass polymer consequently(7) . The drug's bind-ability (Q) values were calculated based on the initial concentration values to know the amount of heroin retention in the MIPs , which is an indication of the selectivity of the heroin- MIPs , and this was then fixed in the table 4 and 5.

Table 4. Heroin-MIP particles based on acrylamide are used to rebind heroin values

Heroin _MIP(acrylamide)						
Mass of MIP g	**Constriction ppm**	**Ci mM**	**C_{free} mM**	**Q µMole /g**	**Q/C_{free} L/g**	**T: P (templet: polymer)**
0.2	**20**	**0.2010**	**0.1875**	**2.9783**	**15.8842**	**1:4**
	40	**0.4020**	**0.6527**	**3.8743**	**5.9358**	**1:2**
	60	**0.6030**	**0.5985**	**2.8234**	**4.7174**	**1:6**
	80	**0.8040**	**0.6921**	**2.729**	**3.943**	**1:4**
0.4	**20**	**0.2010**	**0.1853**	**1.8954**	**10.2288**	**1:8**
	40	**0.4020**	**0.2329**	**3.8743**	**16.635**	**1:4**
	60	**0.6030**	**0.3723**	**3.8358**	**10.3029**	**1:2**
	80	**0.8040**	**0.2623**	**3.4286**	**13.071**	**1:2**

Table 5. Heroin-MIP particles based on n-iso propyiacrylamide are used to rebind heroin values

Heroin_MIP(n-iso propyiacrylamide)						
Mass of MIP g	**Constriction Ppm**	**Ci mM**	**C_{free} mM**	**Q µMole /g**	**Q/C_{free} L/g**	**T: P (templet:polymer)**
0.2	**20**	**0.2010**	**0.2832**	**0.028**	**0.0988**	**1:8**
	40	**0.4020**	**0.3842**	**0.2904**	**0.7558**	**1:6**
	60	**0.6030**	**0.5639**	**0.3219**	**0.5708**	**1.2**
	80	**0.8040**	**0.7492**	**0.3843**	**0.5129**	**1:6**
0.4	**20**	**0.2010**	**0.1854**	**0.7843**	**4.2509**	**1:4**
	40	**0.4020**	**0.3732**	**0.9832**	**2.6345**	**1:4**
	60	**0.6030**	**0.5754**	**1.7329**	**3.0116**	**1:8**
	80	**0.8040**	**0.7943**	**1.3481**	**1.6972**	**1:2**

Heroin-MIP based on acrylamide and n-iso propyiacrylamide exhibits a two-site non-covalent bond connection with the polymer through isotherm adsorption. Heroin-MIP's scat chard plot showed nonlinearity with acrylamide and n-isopropyiacrylamide, suggesting that the binding sites differed depending on heroin. Each of the two distinct sections of the plot is depicted by a straight line with a corresponding equation. This suggests that the polymer has two different kinds of heroin binding sites Fig 2and 3. We suggest that heroin attaches to acrylamide and n-isopropyiacrylamide through the two oxygen atoms in the polymer (21).

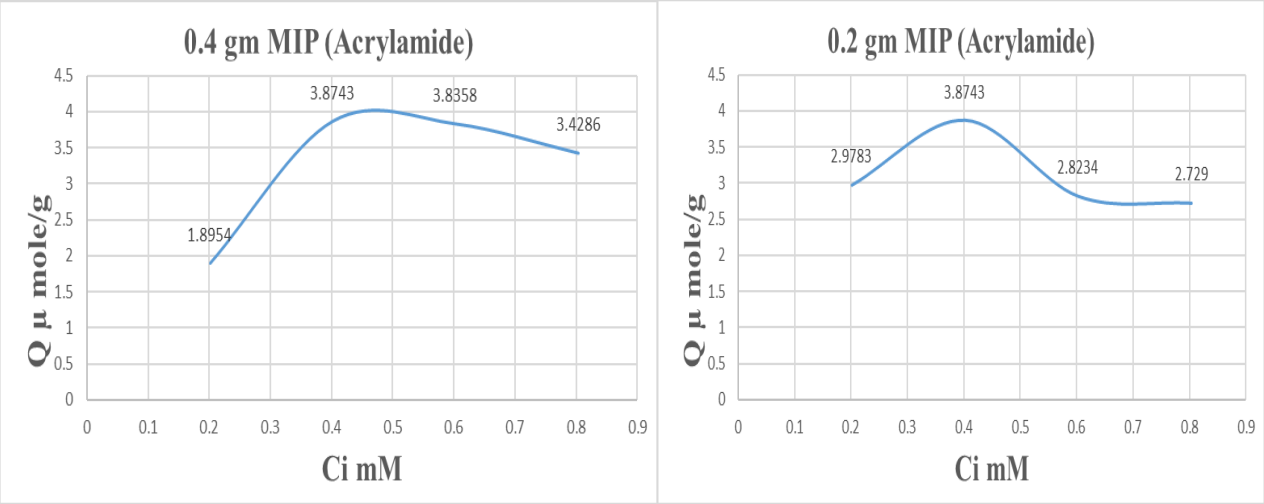


Figure 2. Plotting Q against Ci to determine the acrylamide monomer's binding isotherm

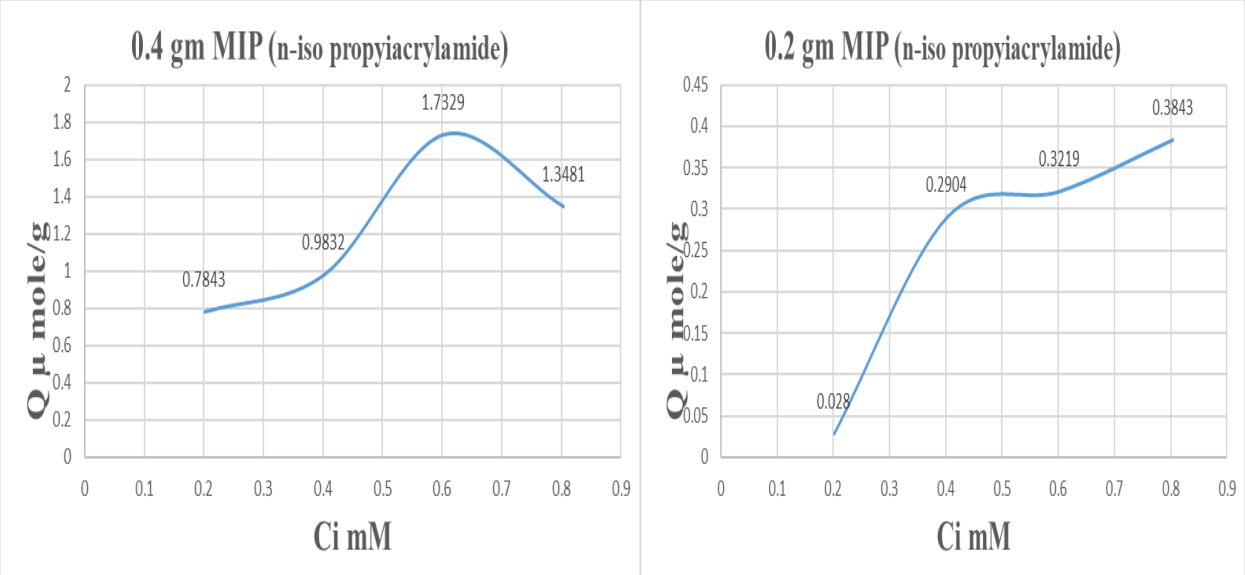
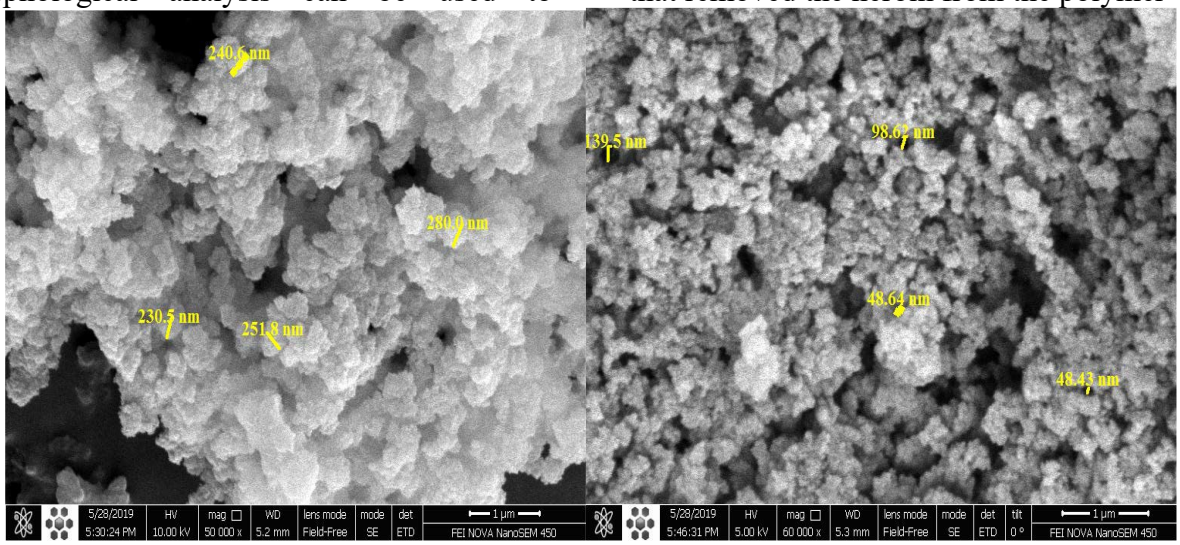


Figure 3. Plotting Q against Ci to determine the n-iso propyiacrylamide monomer's binding isotherm

Characterization of morphological: Morphological analysis can be used to determine the size and arrangement of the sites that removed the heroin from the polymer



A **B**

Figure 4- SEM image of the morphine-MIP surface (A-acrylamide and B-n-isopropyiacrylamide)

Heroin-MIP powders successfully hybridized into polymer membranes, as seen by the SEM pictures in Fig.4; the printed membranes had a flat surface. Furthermore, morphological research revealed that Heroin-MIP (n-iso propyiacrylamide) has a higher spherical structure than morphine-MIP (acrylamide). The tiny, spherically formed polymeric particles discovered in microanalysis are depicted in the matching image in Figure 5. These particles' sizes range from 230.5 to 280 nm for acrylamide polymer and from 48.64 to 139.5 nm for n-iso propyiacrylamide polymer.Analysis of urine samples. MIP-acrylamide was evenly sprayed, and under ideal conditions, MIP-n-iso propyiacrylamide was applied using a Freundlich isotherm to identify heroin in urine samples. Both the initial process and the post-extraction wash phase made use of the urine sample matrix. A peristatic pump will be used to finish the cleaning process so that the carrier and solution can flow through the plastic syringe. Substances that weakly suck into a homogenous column should be eliminated during the washing stage. It was shown that in order to decrease the matrix peaks, the washing duration has to be increased from 70 seconds to three minutes. Take a sample of empty urine and wash it for three minutes to demonstrate this. The urine sample had adequate levels of heroin using the same washing method ,there was no drop in In optimal conditions, urine samples were successfully treated with 0.2–0.4 g of MIP (acrylamide) and MIP (n-iso propyiacrylamide) to produce 20–100 parts per million of heroin. The findings are displayed in Table (6).

Table 6. The conventional addition approach for drug detection makes use of solid phase extraction and the imprinted polymer technology

Wt. of MIP(g)	Type of MIP	NO.of patient	Conc. Taken (ppm)	Conc. Found (ppm)	% Recovery	RSD%	RE%
0.2	MIP-	2	40	38	95	3.16	-5
	Acrylamide	2	80	81	101.25	2.83	1.25
0.4		2	40	37	92.5	4.27	-7.5
		2	80	82	102.5	2.92	2.5
0.2	MIP-	2	40	41	102.5	1.94	2.5
	n-iso	2	80	78	97.5	2.71	-2.5
0.4	propyiacrylamide	2	40	38	95	2.16	-5
		2	80	83	103.75	3.24	3.75

From the table(7), we notice when comparing the results obtained with the researchers' results that the statistical values are consistent with them, and this indicates the success of using acrylamide as monomer in detecting heroin (26).=

Conclusion

The MIP-Heroin Solid Phase Extraction (SPE) column was utilized to extract heroin from the urine samples used in this study. The ability of each imprinted polymer to bind heroin and other comparable substances is also known. In order to enhance drug metabolism, making the molecularly imprinted heroin polymers was the initial stage, permitting the detection and concentration of the drug's trace levels at different times. The second step involved obtaining a concentration using solid phase extraction, which enhanced precision, sensitivity, and selectivity. flow rate and sample volume. The time dropped as the flow rate increased when we put it at 70 rpm, and it was 5 minutes at that point. Due to their strong reproducibility and perceived suitability for tracing levels, heroin quantities under 10 mL should be used. To determine if the Freundlich or Langmuir models are isothermal.Very low detection limits of 0.6–1.8 mg mL−1 were attained. Relative recoveries ranged from 92.5 to 103.75%., and MIP fibers were finally successful in extracting heroin-containing urine samples.

CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

DECLARATION OF FUND

The authors declare that they have not received a fund.

REFERENCES

1- Al-Bayati, Y. K. and E. A. Hadi. 2022. Synthesis of new molecularly solid-phase used styrene and allyl chloride base functional

monomer for determination of cocaine by gc-mass and its clinical applications. Iraqi Journal of Agricultural Sciences, 53(4) :760–766. https://doi.org/10.36103/ijas.v53i4.1586.

2- Alexandra, M, Madea, B., and C. Hess, 2018. Confirmation of recent heroin abuse: Accepting the challenge. Drug testing and analysis, 10(1), 54-71. https://doi.org/10.1002/dta.2244

3- Alexandra, M, M. Kraemer, K. Sydow, P. S. Chen, T. Dame, F. Musshoff, and C. Hess, 2017. Urinary excretion study following consumption of various poppy seed products and investigation of the new potential street heroin marker ATM4G. Drug Testing and Analysis, 9(3), 470-478. https://doi.org/10.1002/dta.2058

4- Alyautdin, R., I. Khalin, M. I. Nafeeza, M. H. Haron, and D. Kuznetsov, 2014. Nanoscale drug delivery systems and the blood–brain barrier. International journal of nanomedicine, 795-811. https://doi.org/10.2147/IJN.S52236

5- Abdulameer.J. H. and M. F. Alias.2022 .Heavy Metal Complexes of 1, 2, 3-Triazole derivative: Synthesis, Characterization, and Cytotoxicity Appraisal Against Breast Cancer Cell Lines (MDA-MB-231). Baghdad Science Journal,6(19): 1410-1422. https://doi.org/10.21123/bsj.2022.7178.

6- Al-Bayati, Y. K. 2024. Determination of Morphine Using Molecularly Imprinted Polymers Based on Different Monomers .Iraqi Journal of Agricultural Sciences, 55(4):1557–1565. https://doi.org/10.36103/mkwd9746.

7- Araceli, P, A., E. O. Joekes, and J. C. March, 2007. Nursing in an intravenous heroin prescription treatment. Journal of Addictions Nursing, 18(1), 13-20. DOI: 10.1080/10884600601174425

8- Avram, G, A. 1991. Heroin addiction: neurobiology, pharmacology, and policy. Journal of psychoactive drugs, 23(2), 123-133. https://doi.org/10.1080/02791072.1991.10472231

9-Alhaddad. M. and S. M. Sheta. 2020. Dual Naked-Eye and Optical Chemosensor for Morphine Detection in Biological Real Samples Based on Cr(III) Metal–Organic Framework Nanoparticles.ACS Omega journal,5(43):28296–28304. https://doi.org/10.1021/acsomega.0c04249.

10- Boerner, U., S. Abbott, and R. L. Roe, 1975. The metabolism of morphine and heroin in man. Drug metabolism reviews, 4(1), 39-73. https://doi.org/10.3109/03602537508993748

11-Brink .W.V, V. M. Hendriks, P. Blanken, M. W. J. Koeter, B. J .van Zwieten and J. M. van Ree. 2003 .Medical prescription of heroin to treatment resistant heroin addicts: two randomised controlled trials.National Library of Medicine,310(327):1,6. https://doi.org/10.1136/j.327.7410.310

12- Babiker M. El-Haj, M. A. Abdelkader, H. S. Ali and I. Ahmed .2007. GC-MS detection and characterization of thebaine as a urinary marker of opium use.Forensic Toxicology,25(9):62–68. https://doi.org/10.1007/s11419-007-0028-4.

13- Blum, J., H. Gerber, U. Gerhard, O. Schmid, S. Petitjean, A. Riecher-Rössler, , ... and M. Walter, 2013. Acute effects of heroin on emotions in heroin-dependent patients. The American journal on addictions, 22(6), 598-604. https://doi.org/10.1111/j.1521-0391.2013.12025.xCitations: 33

14-Fischer.B ,J. Rehm, M. Kirst and J. M. van Ree. 2022. Heroin-assisted treatment as a response to the public health problem of opiate dependence.The European Journal of Public Health12(3):228-34. https://doi.org/10.1093/e12.3.228.

15-Hadi, E. A. and Y. K. Al-Bayati. 2022. Preparation and characterized study of new molecularly imprinted polymers for determination Cocaine by GC-Mass based on different functional monomers .Egyptian Journal of Chemistry, 65(1):107–116. https://ejchem.journals.ekb.eg/article_181889.html.

16-Ingmar, F, V. M. Hendriks, C. J. Stam, and W. Van den Brink, 2004. A role for dopamine in the processing of drug cues in heroin dependent patients. European Neuropsychopharmacology, 14(6), 503-508. https://doi.org/10.1016/j.euroneuro.2004.02.004

17- Milella, M. S., G. D'Ottavio, S. De Pirro, M. Barra, D. Caprioli, and A. Badiani, 2023. Heroin and its metabolites: relevance to heroin use disorder. Translational psychiatry, 13(1), 120. https://doi.org/10.1038/s41398-023-02406-5

18- Maas, A., B. Madea, and C. Hess, 2018. Confirmation of recent heroin abuse: Accepting the challenge. Drug testing and analysis, 10(1), 54-71. https://doi.org/10.1002/dta.2244

19-Moros. J., N. Galipienso, R. Vilches, S. Garrigues and M. Guardia. .2008. Nond-estructive Direct Determination of Heroin in Seized Illicit Street Drugs by Diffuse Reflectance near-Infrared Spectroscopy. Analytical Chemistry, 80 (19):7257–7265. https://doi.org/10.1021/ac800781c.

20-Nicole. A, L. W. Simon, N. Barnett, P. James, R. Kirkbride and K. Paul. 2005. The rapid analysis of heroin drug seizures using micellar electrokinetic chromatography with short-end injection.Journal of Forensic Sciences,50(1):37-42. https://pubmed.ncbi.nlm.nih.gov/15830995/.

21- Ning, T., C. Leng, L. Chen, B. Ma, and X. Gong, 2018. Metabolomics analysis of serum in a rat heroin self-administration model undergoing reinforcement based on 1H-nuclear magnetic resonance spectra. BMC neuroscience, 19(1), 4. https://doi.org/10.1186/s12868-018-0404-5

22- Nathan, S, D. Gerostamoulos, J. Gerstner-Stevens, N. Scott, K. Smith, O. H. Drummer, and J. L. Pilgrim, 2018. Determining the effective dose of street-level heroin: a new way to consider fluctuations in heroin purity, mass and potential contribution to overdose. Forensic Science International, 290, 219-226. https://doi.org/10.1016/j.forsciint.2018.07.009

23- Nancy K., and H. Jack Mendelson. 1980. Buprenorphine suppresses heroin use by heroin addicts. Science, 207(4431), 657-659. DOI: 10.1126/science.7352279

24-Nada F. A., A. Galal and S.H. Hassan .2015. Electrochemical Sensor for morphine based on gold nanoparticles/ ferrocene carboxylic acid/ poly (3,4-ethylenedioxythiophene) composite. International Journal of Electrochemical Science10(3):22652280. https://doi.org/10.1016/S14523981(23)04845-9.

25-Pervukhin,.V.V, and D. G. Sheven. 2016. mass-spectrometric study of the aqueous solutions of opiates with their ionization in a collison nebulizer. Journal of Analytical Chemistry,71(9):878–887. https://doi.org/10.1134/S1061934816090112.

26-Smith. M. T. 2000.Neuroexcitatory effects of morphine and hydromorphone: evidence implicating the 3-glucuronide Metabolites .27(7):524-538.

27. Van den Brink, W., Hendriks, V. M., Blanken, P., Koeter, M. W., van Zwieten, B. J., and J. M. Van Ree, 2003. Medical prescription of heroin to treatment resistant heroin addicts: two randomised controlled trials. Bmj, 327(7410), 310. https://doi.org/10.1136/bmj.327.7410.310

28.Zaaijer, E. R., A. E. Goudriaan, M. W. Koeter, J. Booij, and W. van den Brink, 2016. Acceptability of extended-release naltrexone by heroin-dependent patients and addiction treatment providers in the Netherlands. Substance use & misuse, 51(14), 1905-1911.