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МЕТОД ЖХ-МС/МС ДЛЯ ОПРЕДЕЛЕНИЯ МЕЗИЛАТА ИМАТИНИБА В ОБРАЗЦАХ ПЛАЗМЫ КРОВИ ПОСЛЕ АДСОРБЦИИ МЕДНОЙ ДУБИЛЬНОЙ КИСЛОТОЙ

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Новый металлоорганический каркасный сорбент (MOF) на основе дубильной кислоты/меди (TA/Cu) был синтезирован и охарактеризован для применения противоракового препарата иматиниба (IMA) из биологических образцов. TA/Cu MOF был приготовлен с помощью простой координационной реакции и тщательно охарактеризован методами SEM, XRD и FTIR. Были оптимизированы критические параметры, влияющие на эффективность экстракции мезилата иматиниба (IMAM), включая pH, ионную силу, десорбционный растворитель и время адсорбции-десорбции. С ацетонитрилом в качестве десорбционного растворителя метод продемонстрировал широкий линейный диапазон 0,55-300 мкг л$^{-1}$ в идеальных условиях. Было обнаружено, что пределы обнаружения и количественного определения составляют 0,16 мкг л$^{-1}$ и 0,55 мкг л$^{-1}$ соответственно. Для образцов плазмы, в которые были добавлены клинически значимые концентрации (5, 20 и 50 мкг л$^{-1}$), сорбент продемонстрировал хорошую пригодность к повторному использованию в течение четырех циклов и незначительные матричные эффекты. По сравнению с ранее опубликованными методами разработанный метод дисперсионной твердофазной экстракции на основе TA/Cu MOF показал лучшие результаты с точки зрения простоты, коэффициента обогащения и аналитических показателей. Другой целью данного исследования была разработка жидкостной хроматографии с тандемной масс-спектрометрией, которую можно было бы широко и легко использовать для терапевтического мониторинга препарата иматиниб после экстракции твердофазной экстракцией (SPE). Терапевтические приложения мониторинга могут надежно количественно определять IMA в сложных биологических матрицах в результате процедуры быстрой дисперсионной твердофазной экстракции (DSPE) и экологически чистого сорбента.

Ключевые слова: дубильная кислота/медь, дисперсионная твердофазная экстракция, иматиниб, образцы плазмы, ЖХ-МС/МС

LC-MS/MS METHOD FOR THE DETERMINATION OF IMATINIB MESYLATE IN BLOOD PLASMA SAMPLES AFTER ADSORPTION BY COPPER TANNIC ACID

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A novel metal-organic framework (MOF) sorbent based on tannic acid/copper (TA/Cu) was synthesized and characterized for the application of the anticancer drug imatinib (IMA) from biological samples. The TA/Cu MOF was prepared via a facile coordination reaction and thoroughly characterized by SEM, XRD, and FTIR techniques. Critical parameters influencing the extraction efficiency of imatinib mesylate (IMAM), including pH, ionic strength, desorption solvent, and adsorption-desorption time were optimized. With acetonitrile as the desorption solvent, the method demonstrated a broad linear range of 0.55-300 μg L^{-1} under ideal conditions. Limits of detection and quantification were found to be 0.16 μg L^{-1} and 0.55 μg L^{-1}, respectively. For plasma samples spiked at clinically relevant concentrations (5, 20, and 50 μg L^{-1}), the sorbent showed good reusability over four cycles and negligible matrix effects. In comparison to previously published methods, the developed dispersive solid phase extraction method based on TA/Cu MOF performed better in terms of simplicity, enrichment factor, and analytical figures. Another objective of this study was to develop a liquid chromatography with tandem mass spectrometry technique that could be commonly and readily used for therapeutic drug monitoring of imatinib following extraction by solid phase extraction (SPE). Therapeutic monitoring applications can reliably quantify IMA in complex biological matrices as a result of the fast dispersive solid phase extraction (DSPE) procedure and environmentally friendly sorbent.

Keywords: tannic acid/copper, dispersive solid-phase extraction, imatinib, plasma samples, LC-MS/MS

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INTRODUCTION

Uncontrollably multiplying cells are the first step toward cancer in the body. One type of cancer that begins in specific bone marrow is called chronic myeloid leukemia (CML). It is linked to the existence of an aberrant chromosome that displays the BCR-ABL1 fusion gene. An inhibitor of BCRABL1 tyrosine kinase that is selective is called Gleevec, imatinib mesylate (IMAM). It is an antiproliferative agent that inhibits tumor cell proliferation and induces apoptosis; the Food and Drug Administration (FDA) has approved it for use in the treatment of CML [1]. Additionally, it has been observed that this medication is effective in treating gastric stromal malignant tumors (GIST) [2].

Since some useful methods for the quantitative evaluation of the medication have been presented to IMA, there has been an increased focus [3-8]. IMAT levels in patients' bloodstreams differ based on the dosage they take, which could point to a relationship between the drug's potency and the patient's therapeutic response [9]. Earlier reports have indicated that monitoring IMB levels is important for medicine as well as the environment [10].

Recently, solid phase extraction (SPE) has become a routine sample preparation technique that is well-suited for complex biological sample pretreatment, because of SPE's more potent purification ability, diminished matrix effects, and lowered need for organic solvent. Dispersive solid phase extraction (DSPE) is primarily utilized for trace determination of compounds such as benzoylurea insecticides, parabens, and herbicides from various complex matrices [11-13]. Numerous studies have demonstrated the great potential of metal-organic frameworks (MOFs) in sorption-related fields, indicating their potential suitability as effective sorbents for sample preparation techniques like DSPE [14-17].

Analyzing drugs is essential due to the substantial increase in the consumption of drugs around the world and the ensuing effects on the natural environment [18]. The identification of different substances presents a challenge to activists for the environment and biology [19-21]. The products with medicinal properties are increasingly common [22]. Numerous methods for class identification have been studied as a result of the pervasive issue of medication contamination [23]. Spectrophotometric methods are more advantageous for identifying samples from nature due to their low cost and simplicity of use [24-27].

Several analytical methods including gas chromatography (GC) and high-performance liquid chromatography (HPLC) have been employed to determine

the IMAT concentration [5, 28-31]. Despite their great sensitivity and extremely accurate measurements, most of these techniques have drawbacks, such as complicated equipment and the need for knowledgeable and competent operators [32]. Nowadays, one of the most popular techniques is LC coupled with MS/MS, which has significant potential for determining the identity and quantification, high specificity, and stability [33]. Numerous analytes, including macromolecules and small pharmaceutical compounds, have been studied using ionization mass methods [34].

In this study, imatinib mesylate (IMA) was successfully extracted from plasma samples using dispersive solid-phase extraction (DSPE), which used a tannic TA/Cu MOF as the sorbent material. This study also aimed to create a liquid chromatography with tandem mass spectrometry (LC-MS/MS) method that could be easily and typically used for imatinib therapeutic drug monitoring after extraction by SPE.

MATERIALS AND METHODS

Chemicals and reagents

Imatinib mesylate (99.9% purity) was purchased from Merck (Darmstadt, Germany). HPLC-grade acetonitrile (ACN), methanol, and formic acid were provided by Sigma-Aldricht, USA. The water system was supplied by Millipore (Bedford, MA, USA). TA/Cu MOF was obtained from commercial sources.

Instrumentation and analytical conditions

The LC-MS/MS system consisted of a Waters Alliance LC system interfaced with a Waters Xevo TQ tandem quadrupole mass spectrometer. Chromatographic separation was achieved on the symmetry C18 column (100 mm × 4.6 mm i.d., 5 μm particle size). A 90:10 v/v isocratic mobile phase containing 0.1% acetonitrile and formic acid was used at a flow rate of 0.5 mL/min. The injection volume was 30 μL, with the column temperature set at 30 °C. Electrospray ionization (ESI) with a mass spectrometer was used. The cone and desolvation gas flows were set at 150 L/h and 650 L/h, respectively, with a capillary voltage of 3000V. The optimized MRM transitions monitored were m/z 494.10 → 393.83 (cone voltage 55V, collision energy 24V) for imatinib $[M+H]^+$.

Preparation of samples

Plasma samples were sourced from the Blood Transfusion Organization in Tabriz, Iran. To prepare the samples, 1 mL aliquots of plasma were transferred into glass test tubes. Known amounts of imatinib were then spiked into these plasma aliquots to create standard solutions at concentrations of 5, 10, and 50 ng L^{-1}. To precipitate plasma proteins, varying quantities of a 30% w/v zinc sulfate solution were added to the spiked plasma solutions. After centrifugation at 5000 rpm for 5 min. Following this protein precipitation step, the diluted samples underwent the extraction procedure using the DSPE method.

General procedure of extraction

For the DSPE procedure, 15 mg of the TA/Cu MOF sorbent was added to 5 mL of deionized water with a pH ranging from 6 to 8, containing 50 ng L^{-1} of imatinib. This mixture was then vortexed for 6 minutes to facilitate the adsorption of the imatinib analyte onto the MOF particles. After vortexing, the sorbent particles were collected by centrifugation, and the supernatant was carefully decanted. After that, 200 μL of ACN was added to the sorbent particles to desorb the extracted imatinib, and this was vortexed again for 3 min. The sorbent particles were then separated by centrifugation. Finally, 30 μL of the ACN supernatant containing the desorbed imatinib was injected into the HPLC-MS/MS system for analysis.

Synthesis of TA/Cu MOF

The CuTA MOF was synthesized by the reaction between Cu (II) ions and TA. 50 ml of deionized water was used to dissolve 0.250 g of TA and 0.825 g of $CuSO_4.5H_2O$ to create a homogenous solution. The pH of this solution was gradually adjusted to 7.4 by dropwise addition of 2 M sodium hydroxide (NaOH). The reaction mixture was then heated to 50 °C and maintained at that temperature for 4 h. After the reaction time, the resulting TA/Cu MOF product was separated by centrifuge. It was then washed three times by re-dispersing in deionized water followed by ethanol to remove any unreacted precursors or byproducts.

RESULTS AND DISCUSSION

Sorbent characterization

SEM and EDX analysis

The initial step involved morphological studies to investigate the structure of the synthesized nanocomposite. Fig. 1 displays scanning electron microscope (SEM) images of TA/Cu at various magnifications. The images shown in Fig. 1a and b demonstrate that the TA/Cu MOF exhibits randomly oriented, extremely thin structures resembling rice grains. This observation corroborates previous research findings, indicating the successful synthesis of the TA/Cu MOF. Additionally, elemental mapping analysis (Fig. 1c) shows copper, oxygen, and carbon elements within the TA/Cu structure.

FTIR analysis

The subsequent step involved a comprehensive examination of the Fourier-transform infrared (FTIR) spectra of the synthesized sample to validate the synthesis of the TA/Cu MOF. As depicted in Fig. 2a, the

FTIR spectrum of TA/Cu exhibited at 3392.69 cm^{-1} due to the C–OH vibrational mode of the TA linker. Moreover, the active vibrational modes associated with the Cu–O bond were observed at 484.67 cm^{-1} and 600.68 cm^{-1}.

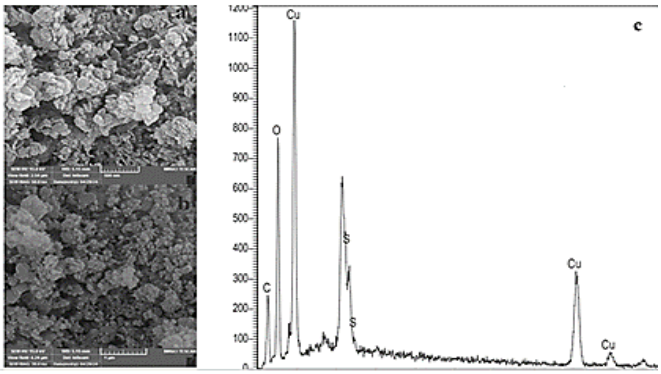

Fig. 1. SEM images of TA/Cu MOF (a and b), EDX spectra of TA/Cu MOF (c)
Рис. 1. Снимки СЭ TA/Cu MOF (a и b), спектры EDX TA/Cu MOF (c)

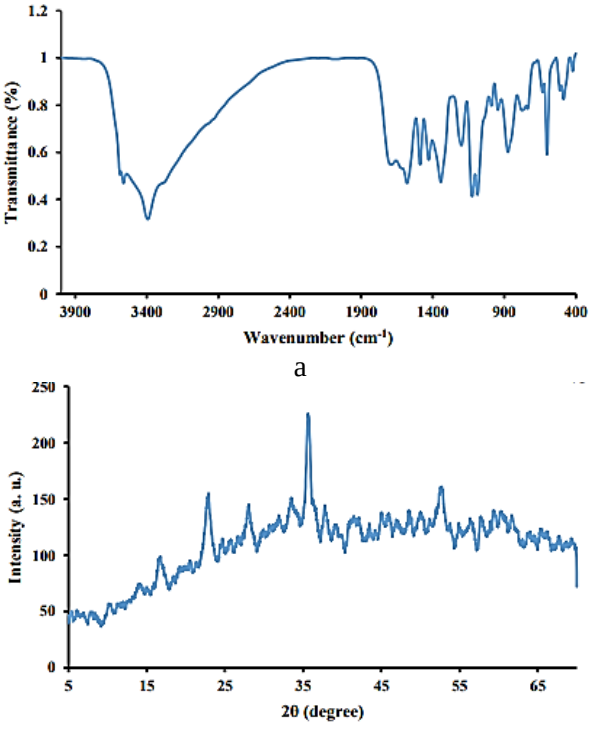

Fig. 2. FTIR spectra of TA/Cu MOF (a), XRD pattern of TA/Cu MOF (b)
Рис. 2. ИК-Фурье спектры TA/Cu MOF (a), рентгенограмма TA/Cu MOF (b)

XRD analysis

XRD analysis was utilized to investigate the structures of the TA/Cu MOF, and the obtained XRD pattern is presented in Fig. 2b. It is anticipated that this process will produce a crystalline MOF structure. There are distinct peaks in the spectrum, especially at 2θ values of about 10°, 18°, 25°, and 33°. The CuTA MOF structure is characterized by these peaks. Terephthalic acid is the organic linker in a copper-based MOF, and the observed diffraction pattern supports this theory. The well-crystallized product indicated by the sharp peaks validates the effectiveness of our synthesis process. A three-dimensional framework structure typical of MOFs is suggested by the presence of multiple well-defined peaks, as opposed to a straightforward copper terephthalate salt. The results of the XRD spectrum are as follows: a) Verifies the creation of a crystalline MOF structure b) Shows that Cu(II) ions and terephthalic acid successfully coordinate c) Enables comparison with previously published CuTA MOF structures in the literature The spectrum displays a good signal-to-noise ratio, suggesting that the sample is crystalline and of high quality. Furthermore, the 200, 400, 600, and 800 planes are represented by the peaks in this XRD spectrum, which are located at roughly 10°, 18°, 25°, and 33° (2θ), respectively. This demonstrates how successful our synthesis and purification techniques are.

Study of effective parameters on extraction efficiency

Evolution of sorbent amount

The efficiency of vortex assisted- dispersive solid phase extraction (VA-DSPE) methods is greatly impacted by the amount of sorbent material used. Increasing the sorbent quantity can potentially enhance extraction efficiency by providing more available adsorption sites. To optimize the method for an imatinib concentration of 50 ng L^{-1}, various sorbent amounts ranging from 2 to 25 mg were investigated, as shown in Fig. 3. The results indicated that maximum extraction efficiency was achieved when using 15 mg of the TA/Cu MOF sorbent. Further increasing the sorbent mass above 15 mg did not lead to any improvement in the extraction recovery of the target imatinib analyte. Consequently, based on these findings, an optimal sorbent amount of 15 mg was selected for subsequent VA-DSPE experiments.

Study of vortex time in the absorption step

Dispersing adsorbent particles in the analyte solution enhances the adsorbent's capability to capture the analyte, leading to improved extraction recovery. This enhancement occurs because the active sites on the adsorbent's surface become more accessible through dispersion, thereby increasing the interaction with the analyte. In this research, a vortex was utilized to disperse the adsorbent particles in the sample solution. The nature and quantity of active sites on the adsorbent's surface and the level of interaction between

the adsorbent and the analyte directly impact the adsorption kinetics, which dictate the required stirring duration for adsorption to occur. By increasing the surface area of the adsorbent and the number of specific analyte binding sites on its surface, the efficiency of interaction between the adsorbent and the analyte is boosted, leading to a reduction in analyte absorption time. This investigation explored absorption times of 2, 4, 6, 8, and 10 minutes, revealing that the highest extraction recovery was achieved at a 6-minute absorption time, Fig. 4.

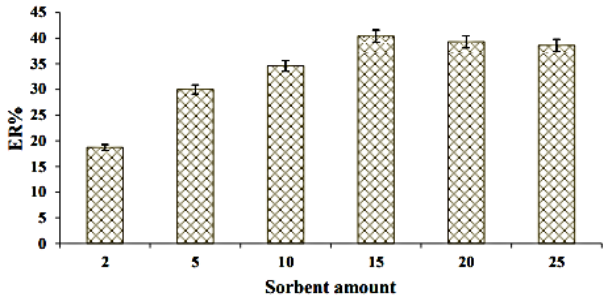

Fig. 3. Optimization of sorbent amount, 5 mL blank plasma samples spiked with 50 ng g^{-1} of imatinib

Рис. 3. Оптимизация количества сорбента, 5 мл контрольных образцов плазмы с добавлением 50 нг $г^{-1}$ иматиниба

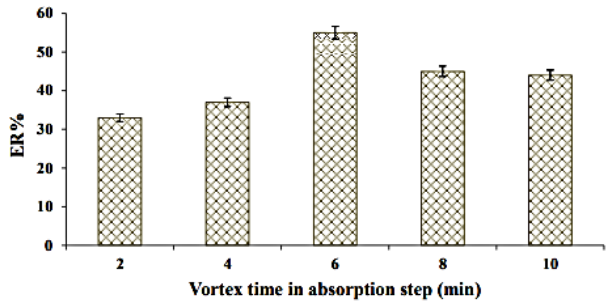

Fig. 4. Vortex time in adsorption step, sorbent amount, 15 mg

Рис. 4. Время вихревого перемешивания на этапе адсорбции, количество сорбента 15 мг

Study of pH effect in the adsorption step

The efficiency of an extraction method is heavily influenced by the pH level. To investigate this effect, multiple solutions containing the same imatinib concentration but differing pH values (2, 4, 6, 8, 10, and 12) were prepared. The results demonstrated that a pH range of 6-8 provided the highest extraction efficiency (Fig. 5). In acidic conditions, imatinib molecules precipitate out and become unstable, leading to reduced extraction recovery. Additionally, under alkaline conditions, the adsorbent's structure likely changes (in other words, deprotonation occurs, decreasing its ability to form hydrogen bonds with the nitrogen atoms of imatinib), which also reduces extraction recovery. Consequently, the extraction process was conducted in a near-neutral pH environment.

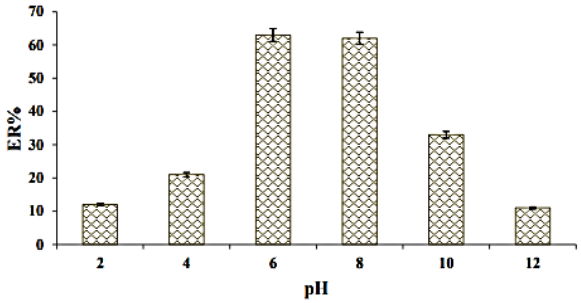

Fig. 5. Study of pH, vortex time, 6 min

Рис. 5. Исследование pH, время вихревого перемешивания 6 мин

Ionic strength effect

To improve the efficiency of the method, the effect of adding salt (NaCl 5% w/v) to the sample solution was investigated, and the obtained results were compared with those from the sample solution without any added salt. The findings (Fig. 6) revealed that the addition of salt led to efficiency. This reduction in efficiency may be attributed to an increase in the solution's viscosity, which impedes the migration process of the analyte towards the active sites on the sorbent's surface. Therefore, the subsequent stages of the study were conducted without the addition of salt to the sample solution.

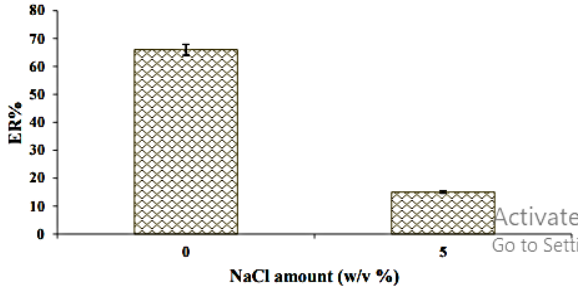

Fig. 6. Salt concentration study, pH, 6-8; and other conditions mentioned in Fig. 5

Рис. 6. Исследование концентрации соли, pH 6-8 и другие условия, указанные на рис. 5

Desorption solvent type and volume

To maximize the efficiency, various solvents including methanol, acetonitrile (ACN), ethanol, and hexanol were evaluated. The results (Fig. 7) demonstrated that ACN solvent yielded the highest extraction performance. This observation could be attributed to the compatibility between the analyte's structure (presence of nitrogen atoms in imatinib) and the polarity of the desorption solvent employed, facilitating enhanced extraction recoveries. Subsequently, the desorption solvent volume was assessed using 100, 150, 200, 250, and 300 μL of ACN. As depicted in Fig. 8, a volume of 200 μL provided the optimal extraction efficiency. Consequently, for the ensuing experiments, ACN solvent at a volume of 200 μL was selected as the ideal condition.

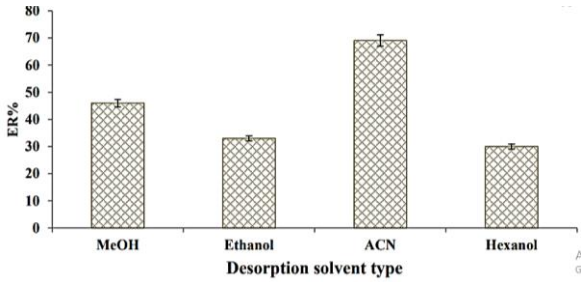

Fig. 7. Elution solvent type, salt concentration, 0% w/v; and other conditions mentioned in Fig. 6

Рис. 7. Тип растворителя для элюирования, концентрация соли 0% (мас./об.) и другие условия, указанные на рис. 6

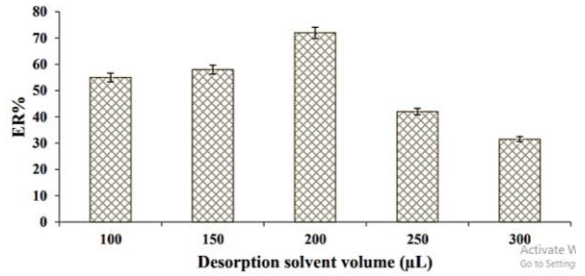

Fig. 8. Elution solvent volume, elution solvent type, ACN; and other conditions mentioned in Fig. 7

Рис. 8. Объем элюирующего растворителя, тип элюирующего растворителя, ACN и другие условия, указанные на рис. 7

Study of vortex time in the desorption step

Optimizing critical factors is crucial for achieving maximum extraction efficiency of analytes. One such pivotal factor is the desorption time, as the effective removal of analytes from the adsorbent enhances their detectable concentration by analytical instruments. Consequently, to boost extraction efficiency, desorption was evaluated over a time range of 0.5 to 6 min. The findings revealed that as the desorption time increased up to 3 min, extraction efficiency peaked. However, beyond this duration, a slight decline in efficiency was observed, potentially attributable to the resorption of the analyte onto the sorbent (Fig. 9). Hence, a vortexing period of 3 min was employed to facilitate optimal analyte desorption.

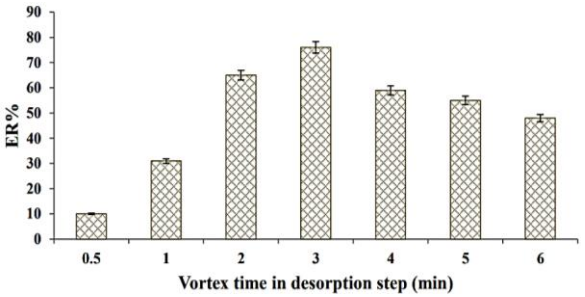

Fig. 9. Vortex time in the desorption step, elution solvent volume, 200 µL; and other conditions mentioned in Fig. 8

Рис. 9. Время вихревого перемешивания на этапе десорбции, объем элюирующего растворителя 200 мкл и другие условия, указанные на рис. 8

Adsorption mechanism

The adsorption of analytes onto the TA/Cu MOF can occur through various interactions, such as hydrogen bonding, electrostatic forces, CH-π interactions, and others, which are directly influenced by the structural characteristics of both the analyte and the TA/Cu MOF. The imatinib molecule possesses an aromatic ring, amine functional groups, and an oxygen atom within its structure. Consequently, the interactions formed can potentially include hydrogen bonding, π-π interactions, and CH-π interactions with the TA ligand present in the TA/Cu MOF framework.

Assessing reusability

To evaluate the performance of the synthesized sorbent, its stability was assessed through a reusability investigation. In each cycle, adsorption and desorption processes were carried out sequentially. After desorbing the analyte, the sorbent underwent thorough washing with 5 mL of ACN to ensure complete removal of any residual analyte. The findings (Fig. 10) demonstrated that the sorbent could effectively extract the analyte up to four consecutive times with minimal variation in the extraction recovery (84.2 ± 4%), indicating its reusability potential.

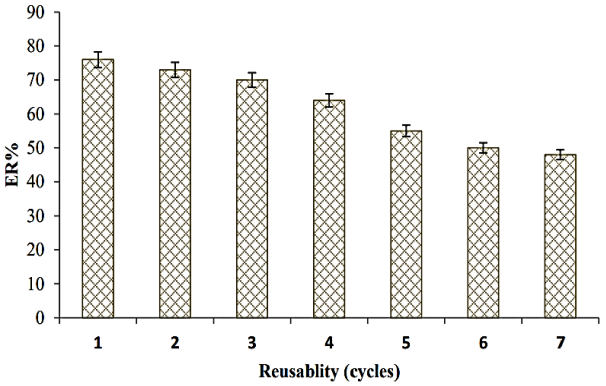

Fig. 10. Reusability, vortex time in the desorption step, 3 min; and other conditions mentioned in Fig. 9

Рис. 10. Возможность повторного использования, время вихревого перемешивания на этапе десорбции 3 мин и другие условия, указанные на рис. 9

Validation of the method

To evaluate the effectiveness and efficiency of a measurement technique, it is crucial to evaluate specific parameters. These parameters serve as indicators of the method's performance or limitations. For instance, by examining factors such as the linearity, coefficient of determination (r^2), limit of quantification (LOQ), limit of detection (LOD), extraction recovery (ER), and precision (determined through repeated experiments and expressed as relative standard deviation), the proposed method can be validated. The aforementioned parameters were presented in Table 1, with

the following considerations: (i) LOD and LOQ were determined using signal-to-noise ratios of 3 and 10, respectively; (ii) the calibration curve (constructed using the proposed method in section 2.4 with standard solutions of varying analyte concentrations) provided the corresponding values for the r^2 and LR; and (iii) relative standard deviation (RSD) was assessed in two ways: intra-day (n = 6) and inter-day (n = 6) precisions. Based on the results, it can be concluded that the proposed method is efficient.

Study of stability

As part of this research, the stability of imatinib was evaluated under short-term temperature and freeze-thaw conditions. To assess its stability at room temperature (short-term temperature), a portion of the quality control (QC) samples was stored at 24 °C for 6 h before undergoing analysis. To investigate the analyte's freeze-thaw stability, the samples underwent three cycles of freezing at -20 °C and thawing at 24 °C, followed by subsequent analysis. The results obtained from these stability tests were compared to those of QC samples. The calculated RSD values for samples with concentrations of 50 and 100 mg mL^{-1} (n = 3) were below 10%, indicating that the desired analyte exhibited stability under the evaluated short-term temperature and freeze-thaw conditions.

Analytical applications

The potential matrix effect and applicability of the synthesized sorbent for real samples were evaluated by analyzing spiked human plasma samples at three concentration levels (5, 20, and 50 ng L^{-1}), following the method described in section 2.4 under optimal conditions. The results, summarized in Table 2 as relative recovery percentages (RR%), demonstrated acceptable RR values ranging from 84% to 93%. These findings indicate a negligible matrix effect in the analyzed samples and suggest that the sorbent can be employed as an efficient and selective adsorbent for the analysis of imatinib in plasma samples.

Comparative evaluation of the proposed method

The capabilities of the studied method were assessed by comparing the parameters such as LOD, EF, and RSD with similar previously reported methods. An examination of the comparative results in Table 3 revealed that parameters like LOD, RSD, and EF of the proposed method. Other advantages of the proposed approach include a short adsorption and desorption time, an acceptable ER, and simplicity. The comparison of these aspects demonstrates that the proposed method possesses the potential and practicality for application in SPE methodologies.

Table 1

Analytical characteristics of the proposed method for imatinib

***Таблица 1.* Аналитические характеристики предлагаемого метода для иматиниба**

Analyte	LOD (μg L^{-1})	LOQ (μg L^{-1})	Linear range (μg L^{-1})	r^2	Intra-day (n = 6)	Inter-day (n = 6)	ER ± SD
Imatinib	0.16	0.28	0.55-300	0.993	4.8	6.1	76 ± 4

Table 2

Determination of imatinib in plasma samples

***Таблица 2*. Определение иматиниба в образцах плазмы**

Sample	Added (μg L^{-1})	found ± SD (μg L^{-1})	RR % ± SD
Plasma	0.00	ND	-
	5.00	4.2 ± 0.25	84 ± 5
	20.00	18.2 ± 0.80	91 ± 4
	50.00	46.5 ± 2.00	93 ± 4

Table 3

Evaluation of the proposed method

***Таблица 3.* Оценка предлагаемого метода**

Sample	LOD (μg L^{-1})	RSD (μg L^{-1})	EF (μg L^{-1})	Method	Refs
Plasma	3	< 11.9	10	SPE-HPLC-UV	[35]
Plasma	6.24	7.71	54	ILS-RHF-CE [e)]	[36]
Plasma	0.33	< 11.9	10	LLE-HPLC-ESI-MS/MS	[37]
Plasma	0.16	< 6.1	25	VA-DSPELC-MS/MS	Current study

The following equations were used to calculate the parameters mentioned:

$$EF = C_{sed}/C_0 \quad (1)$$

$$\%ER = EF \cdot \frac{V_{sed}}{V_{sam}} \cdot 100 \quad (2)$$

EF and ER are defined, respectively, as the ratio of the analyte concentration in the sedimented phase

(C_{sed}) to its initial concentration in the aqueous phase (C_0) and as a percentage of the total amount of analyte extracted in the settled phase. In equation (2), the terms V_{sed} and V_{aq} refer to the volume of the sedimented phase and the aqueous phase, respectively.

RR% is defined using the following equation:

$$Relative\ Recovery = \frac{C_{found}}{C_{add}} \cdot 100 \quad (3)$$

In equation (3), the terms C_{found} and C_{add} represent the concentration of IMA found and added in plasma samples respectively.

CONCLUSION

In this study, a TA/Cu MOF was synthesized by the reaction between Cu ions and TA. The successful synthesis of the sorbent was confirmed using SEM, XRD, and FTIR techniques. By optimizing the experimental conditions and investigating relevant parameters, the results demonstrated that the synthesized sorbent exhibited good adsorption capacity, high ER, acceptable reusability, and stability. Moreover, the prepared sorbent showed significant potential for application in the VA-DSPE method for the separation of the target analyte.

The authors declare the absence of a conflict of interest warranting disclosure in this article.

Авторы заявляют об отсутствии конфликта интересов, требующего раскрытия в данной статье.

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