Preparation of polyfam/Metal-organic framework electrospun nanofiber as an efficient nanosorbent for micro solid phase extraction of three anticancer drugs followed by chromatographic analysis

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1 Introduction

Over the past several years, a new generation of cancer treatment has come to the forefront, i.e, targeted cancer therapies. As the name suggests, targeted therapies interfere with specific proteins associated with tumors . However, still due to considerable off-tumor toxicity, *quantification* of these drugs in:

- human body: to achieve optimal treatment results and
- wastewaters: to prevent their release into the environment

is indispensable.

The analysis of biological fluids such as serum, plasma and urine are commonly associated with the presence of *various biologically active species*, including PROTEINS, SALTS, LIPIDS, and the other compounds that can have a significant influence on the quantification of target analytes. Therefore, *sample pre-treatment step* prior to analysis by analytical instrument is needed.

Herein, an ELECTROSPUN composite, consisting of *polyfam* and a *Co-metal organic framework- 74*, was developed as a novel sorbent for the high-throughput micro solid-phase extraction of certain anti-cancer drugs (*Sorafenib, Dasatinib*, and *Erlotinib* hydrochloride) from wastewater and biological samples before high-performance liquid chromatography- ultraviolet analysis (HPLC-UV).

The synthesis of the resulting composite nanofibers was confirmed using the techniques of:

- field emission scanning electron microscopy (FESEM) and,
- X-ray diffraction analysis
- Fourier Transform Infrared Spectroscopy (FT-IR)

Thanks to the incorporation of Co-MOF-74 into the polyfam network, the electrospun nanofibers displayed a large surface area, high porosity, and significant extraction efficiency toward target analytes. Under optimal experimental conditions.

2 Objectives

Since **tumor-selective drugs** are yet to be developed and therefore, normal cells can be influenced by off-tumor on-target cytotoxic activity of these drugs, *precision dosing* is conducted as a crucial and valuable step prior to prescribing such drugs in order to optimize the plasma concentration of the drug and subsequently, its clinical effects without altering the overall health condition of the patient. Thus, quantifying trace amounts of anti-cancer drug residues in biological fluids can be considered to provide valuable data for this step. In addition to their direct effects, these drugs must be quantified in wastewaters as well, in order to monitor and prevent their release into the environment.

Direct determination of these analytes at TRACE concentration levels in different biological samples faces challenges owing to the MATRIX EFFECT, and other interferences in samples that tend to restrain their determination [1].

Micro-solid phase extraction (µSPE) based on *Polyfam/Co-MOF-74* composite nanofibers is a MINIATURIZED format of conventional SPE, which only requires few MILLIGRAMS of the ADSORBENT, bringing the advantage of lowered consumption of hazardous organic solvent and reagent.

In this method, the extraction can be more facile and shorter than conventional solid phase extraction (SPE). To the best of our knowledge, there is no report on the coextraction of these drugs using polyfam/Co-MOF-74 sorbent based on µSPE method.

3 Material and Methods

Experimental Details

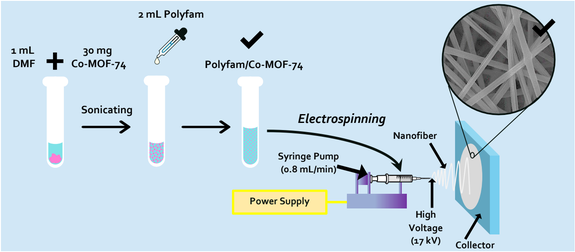
❑ ***Reagents and Materials***

Polyfam 620 (brownish liquid, density = 1.11 ± 0.01) was purchased from Resinfam Co. (Tehran, Iran, info@resinfam.com). SORA (pK_a = 11.55; Log *P* = 4.34), DASA (pK_a = 8.51; Log *P* = 3.83) and ERLO (pK_a = 16.14; Log *P* = 3.2) were graciously donated by Parsian Pharmaceutical Technologists (Karaj, Iran) and used without any purification.

❑ ***Preparation of electrospun polyfam/Co-MOF-74 composite nanofibers***

The composite of polyfam nanofibers with MOF was formed by using the ELECTROSPINNING method.

- First, 30 mg (1.5% w/w) of Co-MOF-74 powder was dispersed in 1.0 mL of DMF by sonicating, and
- then, 2.0 mL of polyfam was added drop by drop to the above solution and stirred for 4 h to obtain a homogenized solution.
- The final solution was drawn into a 3-mL syringe with a steel needle. Between the collector and the needle tip, the applied voltage was constantly 17 kV, and the distance was adjusted to 9 cm. Also, the flow rate was adjusted to 0.8 mL h^{-1}. After 2 and half hours, the electrospun nanofibers were obtained with the desired thickness.
- In the end, the aluminum foil with polyfam/Co-MOF-74 nanofibers was removed from the collector and exposed to the air overnight in order to remove the solvent from the sorbent surface.



❑ ***µ-SPE procedure***

First, a piece of sorbent with the dimension of 1×1 (cm×cm, 3.3 mg) was cut from the nanofiber sheet and submerged in 10 mL of ACN for 10 min to condition it before usage.

Then, the fiber was removed from the ACN, and for adsorption, immersed in 20 mL of a sample solution (optimum pH 10) containing 1.0 mg L^{-1} of each analyte while being stirred on the stirrer (300 rpm) for 10 min.

After finishing the adsorption process, the sorbent was transferred into a small glass vial by a pincet, and 500 µL of 0.01 mol L^{-1} NaOH in MeOH was added as the desorption solvent. Then the vial was shaken on the vortex device at the speed of 2500 rpm in 7 minutes to complete the desorption process.

When the time for desorption was up, the eluent solvent was transferred into a vial, and 20.0 µL of it was injected into the HPLC system. **Fig. 2** displays HPLC-UV chromatograms of *non-spiked* and *spiked* wastewater and plasma sample after performing extraction procedures under the opted conditions.

4 Results

❑ **Surface morphology analysis**

The morphologies of synthesized Co-MOF-74 microparticles, electrospun polyfam nanofibers, and electrospun polyfam/Co-MOF-74 composite nanofibers were investigated via using FE-SEM, which are shown in Fig. 1:

- The FE-SEM images of Co-MOF-74 shown in Fig. 1(a, b, and c) indicate that the crystals of Co-MOF-74 were uniform with the micrometer scale.
- Fig. 1(d) presents the morphology of pure polyfam nanofibers, which had a smooth and uniform surface with a small range of diameter from 81 to 126 nm.
- The morphology of polyfam/Co-MOF-74 composite nanofibers is shown in Fig. 1 (e and f), displaying that the diameter of nanofibers have been increased by adding MOF to the polymer solution and the nanofibers exhibit a smooth and beadles structure with significant porosity and surface area [2].

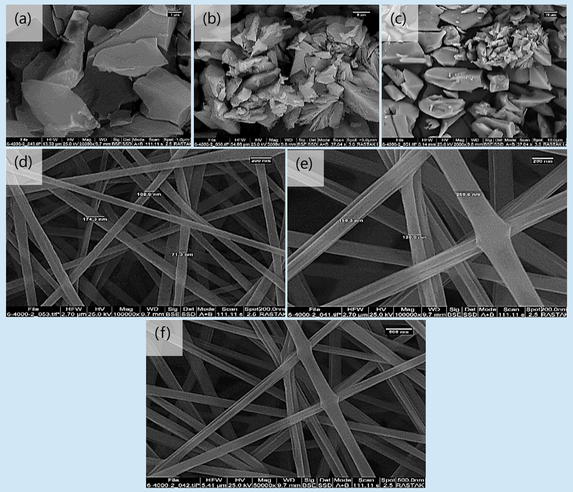


Fig. 1: FE-SEM images of synthesized Co-MOF-74 **(a, b, and c)**; polyfam nanofibers **(d)**; polyfam/Co-MOF-74 composite nanofibers at **(e and f)** at different magnifications.

❑ **HPLC-UV chromatograms of real samples**

As it is exhibited in **Fig. 2**, the results demonstrated that the method has a good potential for detection and enrichment of anti-cancer drugs in different complicated samples.

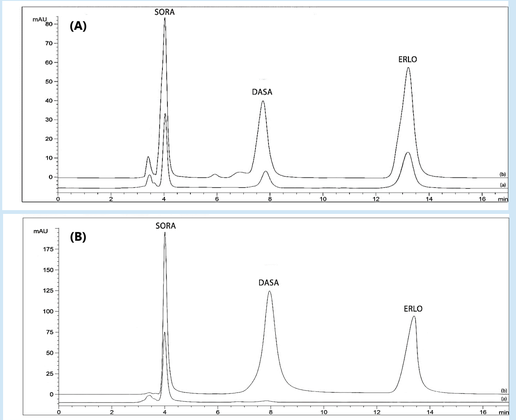


Fig. 2: The chromatograms of **(A)** wastewater sample **(a)** before spiking, **(b)** spiked at 75 µg L^{-1} of each analyte and **(B)** plasma sample **(a)** before spiking, **(b)** spiked at 100 µg L^{-1} of each analyte after µ-SPE.

5 Conclusion

In summary, the composite of polyfam/Co-MOF-74 nanofibers was synthesized through a facile *electrospinning* approach and used as a novel and effective adsorbent in the µ-SPE-HPLC-UV method for the **simultaneous extraction and quantification of three anti-cancer drugs from wastewater and biological samples**. The electrospun composite nanofibers presented a large surface area, good physical and chemical stability, and extraction efficiency. F*Compared with the few reported SPE methods for the target analytes, the µ-SPE method using polyfam/Co-MOF-74 nanofibers provided better analytical performance in LODs, LDRs, and RSDs %.* Furthermore, the developed method can be regarded as an **ECO-FRIENDLY** one since it benefits from **low consumptions of organic solvent and nano sorbent**. Thereby, the composite of polyfam/Co-MOF-74 can be introduced as a promising and efficient sorbent to extract the trace level of anti-cancer drugs in complex matrices.

References

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