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Molecularly Imprinted Polymers/Metal-Organic Framework (MIL-53) for Fluorescent Sensing of Ciprofloxacin in Water†

Monika Nehra[1,2,*] Anjali[2], Nisha Beniwal[2], Neeraj Dilbaghi[2], Rajesh Kumar[1] and Sandeep Kumar[2,3]

[1] Department of Mechanical Engineering, UIET, Panjab University, Chandigarh, 160014, India;
[2] Department of Bio and Nano Technology, Guru Jambheshwar University of Science and Technology, Hisar-Haryana, 125001, India
[3] Physics Department, Punjab Engineering College (Deemed to be University), Chandigarh 160012, India
* Correspondence: ssmonikanehra@gmail.com
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Abstract: The contamination of water and food with antibiotics residues poses a severe risk to human health and aquatic environment. The excessive and uncontrolled use of antibiotics is one of the major causes of their presence in the environment. Their continuous consumption willingly or unwillingly can result in severe health issues such as allergy, headache, hypertension, muscles pain, and hormonal dysfunction. Besides these, the development of antimicrobial resistance (AMR) can make the situation more critical. Therefore, advanced analytical approaches over conventional techniques are required to detect antibiotics residues in a facile and cost-effective manner. Present work deals with design of fluorescent nanostructures as sensing probes for detection of ciprofloxacin. Here, we have synthesized NH_2-MIL-53(Al) using hydrothermal approach. This fluorescent metal-organic framework (MOF) was further combined with molecular imprinted polymers (MIPs) for selective and specific detection of ciprofloxacin in aqueous solutions. The use of MIPs over other biomolecules (such as antibody, enzymes, and others) is highly promising that avoids any kind of pre-treatment of sample. The MIP@NH_2-MIL-53(Al) nanostructure formation is confirmed by different characterization techniques involving both spectroscopy and microscopy. The performance of developed fluorescent composite promotes its applicability for highly sensitive and specific detection of ciprofloxacin in practical applications.

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1. Introduction

All over the world, the emergence of antibiotics in the environment has been recognized as a serious threat to both humans and the ecosystem. There accumulation in water resources can lead to several health issues and endanger the aquatic life. The prolonged exposure of antibiotics in the environment can cause the development antimicrobial resistance (AMR). In such condition, the treatment of simple bacterial infections will be no longer possible. As per the World Health Organization (WHO) report [1], AMR is among the top global major public health threats that require urgent multisectoral action. Therefore, it is highly desirable to develop facile strategies for monitoring the presence of antibiotics in aqueous solutions. Among different antibiotics, ciprofloxacin (with broad-spectrum antibacterial activity and lower side effects) is extensively used to treat urinary tract infections, lung infections, cell carcinoma, and cystic fibrosis [2,3]. However, unintentional exposure and further accumulation of this in human body can cause serious health issues such as hematuria, gastrointestinal complaints, skin reactions, and liver damage [4,5]. Among different conventional techniques like (chromatography, spectrofluorimetry, electrophoresis, electrochemical, etc.), fluorescence approach is a promising method due to its ease of operation, quick response, low cost, and high sensitivity [6–8].

Nowadays, different fluorescent materials, especially metal-organic frameworks (MOFs), have been developed to replace the fluorescent dyes. MOFs offer several unique photophysical properties such as large surface area, structure tunability, photostability,

high porosity, and narrow fluorescence emission. Several research reports explored the fluorescent MOFs for detection of ciprofloxacin. For instance, An et al. [9] reported the Tb-based coordination polymer (CP) for fluorescent detection of ciprofloxacin. Here, ciprofloxacin offered a sensitization effect on luminescence of Tb^{3+}. Besides water and milk samples, the Tb-based complexes have also been reported for ciprofloxacin detection in urine samples [10]. However, the toxic nature of lanthanides can limit their application for real-field monitoring. Liu et al. reported the Zr-based MOF functionalized with citrate (C-MOF-808) for fluorescent detection of ciprofloxacin in aqueous solutions [11]. Besides high sensitivity of these fluorescent sensors, their combination with molecularly imprinted polymers (MIPs) can offer specific target detection capabilities [12,13]. The incorporation of MIPs into porous MOFs can support the excellent selective detection capabilities. High surface area and availability of abundant pores in MOFs is highly favorable for synthesis of imprinting sites. However, there is very limited literature on the use of this combination of MOFs and MIPs for detection of antibiotics. Herein, Al-based MOFs was developed first via hydrothermal approach and later it was combined with ciprofloxacin-specific MIPs. The fluorescent properties of both NH_2-MIL-53(Al) and its composite with MIPs were examined for specific detection of ciprofloxacin.

1. Materials and Method

2.1. Materials

Aluminium(III) chloride hexahydrate ($AlCl_3.6H_2O$), *N*,*N*-dimethylformamide (DMF), 2-aminoterephthalic acid (NH_2-BDC), and ciprofloxacin were purchased from Sigma-Aldrich. Urea, tetraethoxysilane (TEOS), aminopropltriethoxysilane (APTES), and ethanol were procured from HiMedia Pvt. Ltd. Ammonia solution was purchased from E. Merck Ltd. All these analytical grade chemicals were utilized as received without any kind of purification. Distilled water (DW) was prepared in laboratory using distillation unit.

2.2. Synthesis of NH_2-MIL-53(Al)

Al-based MOF was synthesized via hydrothermal approach, earlier reported literature [14]. In detail, 0.3 M $AlCl_3.6H_2O$ was dissolved in 10 mL DW and was mixed in NH2-BDC solution (0.2 M, 15 mL DMF) under continuous stirring. After 10 min, 5 mL aqueous solution of Urea (1 M) was dropped in the above solution and the mixture was stirred for another 10-15 min. Thereafter, the solution was poured to Teflon-lined autoclave and heated to 150 °C for 6 h. The collection of resulting yellow precipitates was done with the help of centrifugation at 9000 rpm for 15 min and were further washed with DW. For activation, the synthesized product was redispersed in 20 mL methanol and DMF solution under dark stirring for overnight. The final produce was centrifuged and dried at 80 °C. The resultant product was collected for further characterization.

2.3. Synthesis of NH_2-MIL-53(Al)/MIP

NH_2-MIL-53(Al)/MIP nanocomposite was prepared by a sol-gel approach [15,16]. Briefly, the aqueous solution of above synthesized MOF (30 mg) and ethanol (10 mL) were added in a reagent bottle. Then, 0.1 mL APTES was added in the above solution under magnetic stirring for self-assembly of APTES over MOF structure. Further, template ciprofloxacin solution (1 mg/mL) was added in the above solution and allowed to stir for 20 min. Next, a drop of ammonia hydroxide was added, followed by dropwise addition of TEOS (1 mL) and ethanol (10 mL). After overnight stirring of this reaction mixture at room temperature, the final product was collected by centrifugation. The product was washed thoroughly with DW and ethanol in subsequent steps upto five times. The final product was dried and stored for further characterization.

2.4. Fluorescence Detection of Ciprofloxacin

In this experiment, the PL of synthesized material (0.02 mg.Ml^{-1}) was examined with varied excitation from 290 to 390 nm. The emission was recorded in between 350 to 450 nm at fixed excitation of 330 nm. The PL of the materials was also studied in the presence of ciprofloxacin (100 µM and 1000 µM) with a 3:1 ratio of ciprofloxacin and MOF or MOF/MIP.

2.5. Characterization of NH$_2$-MIL-53(Al) and NH$_2$-MIL-53(Al)/MIP

The crystalline structure of NH$_2$-MIL-53(Al) was studied by an X-ray diffractometer (Rigaku Ultima diffractometer, USA). The analysis of porosity and surface area of synthesized MOF was done with the help of Belsorp Max system (Microtrac). Hydrodynamic diameter and zeta potential of synthesized structure were also analyzed using Zeta Sizer (Malvern Instruments). The UV-Vis absorption characteristics of NH$_2$-MIL-53(Al) and its composite with MIP were recorded using Shimadzu UV-3600 spectrometer. The functional groups over surface of synthesized materials were studied using Fourier transform infrared (FTIR; Perkin Elmer) spectroscopy. The morphology and topography of the materials were examine using Field emission-scanning electron microscopy (FESEM; JSM6100, Jeol) along with energy dispersive X-ray (EDX) spectroscopy. Fluorescence of the materials were recorded using SpectraMax® system (Molecular Devices).

3. Results and Discussion

The synthesized NH$_2$-MIL-53(Al) is well crystallized as confirmed by the XRD pattern, Figure 1a. All prominent characteristic peaks are in well accordance with literature [17]. Using Debye Scherrer equation, the crystallize size of NH$_2$-MIL-53(Al) was calculated 24.34 nm with a lattice strain of 0.0186. The N_2 adsorption/desorption isotherms of the synthesized MOF are presented in Fig. 1b. The surface area of the MOF using BET method was found 630.24 m^2.g^{-1} along with an average pore diameter of 4.126 nm and a total pore volume of 0.6501 cm^3.g^{-1}. The hydrodynamic diameter of the MOF was found ~483 nm with a polydispersity index of 0.573. The highly positive zeta potential (20.2 mV) of NH$_2$-MIL-53(Al) confirms its aqueous stability that tend to avoid agglomeration.

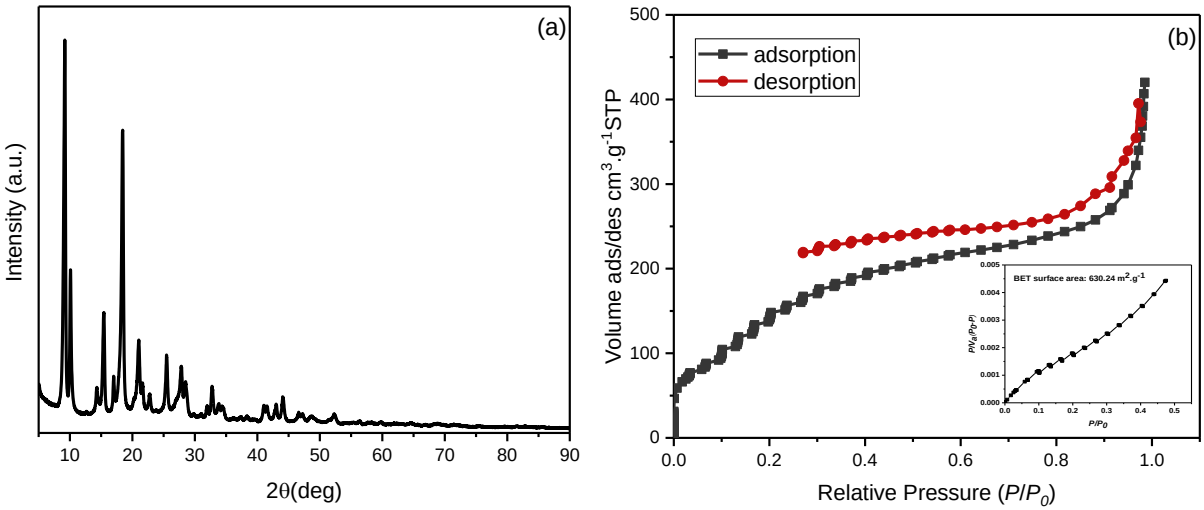

Figure 1. Characterization of synthesized NH$_2$-MIL-53(Al) (**a**) XRD pattern and (**b**) Nitrogen adsorption/desorption isotherms (inset: BET plot) from N2 isotherm at 77.350 K.

In UV-Vis spectra (Figure 2a), two absorption peaks were found for of NH$_2$-MIL-53(Al) at 270 and 380 nm. The absorption peak at 380 nm changes to 330 nm after interaction of NH$_2$-MIL-53(Al) with MIPs. Figure 2b shows the fluorescence spectra of both compounds at a fixed excitation of 330 nm. The interaction of MIPs with MOF structure results the small quenching of fluorescence of MOF. The fluorescence of both compounds is also

studied as a function of varied excitation, refer to Figure 2c. In FTIR spectra (Figure 2d), the broad adsorption band centered at 3462.05 cm^{-1} confirms the presence of OH group in the framework. The peak at 1628.18 cm^{-1} can be allotted to N-H bending [18]. Typical vibration due to benzene linker was observed at 1450.09 cm^{-1} that can be attributed to aromatic ring stretch amines. A significant impact of MIPs can be seen over the presence of functional groups of MOf. The size of as synthesized MOF was found within 100 nm range with shape symmetry, refer to Figure 3a. The uniform distribution of MOF with MIP can be seen in Figure 3b. EDS spectra of both compounds are presented in Figure 3 c,d.

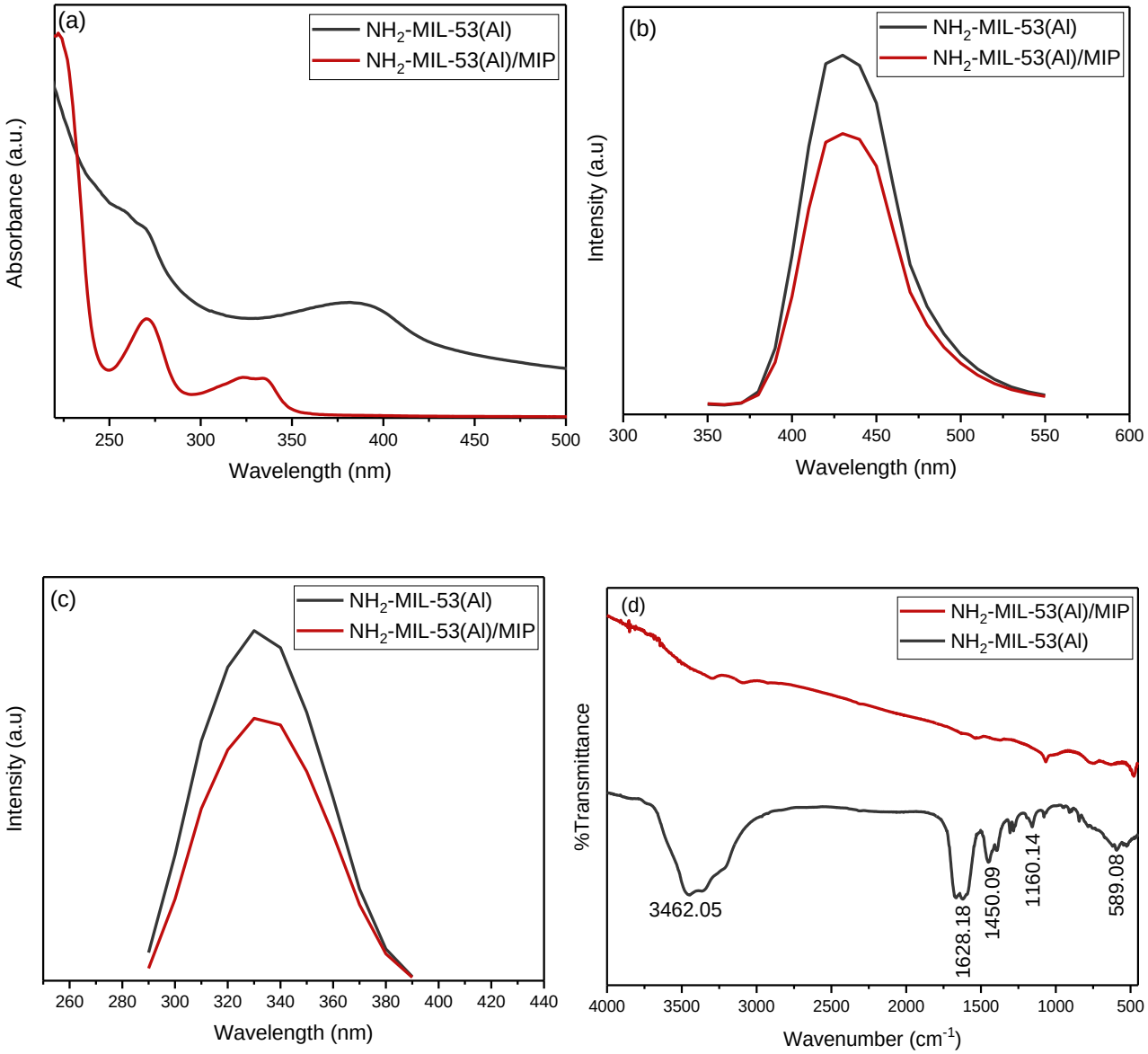

Figure 2. Optical characteristics of NH_2-MIL-53(Al) and NH_2-MIL-53(Al)/MIP (**a**) UV-Vis absorption, (**b**) fluorescence emission spectra at fixed excitation of 330 nm, (**c**) fluorescence emission spectra with varied excitation and fixed emission at 430 nm, and (**d**) FTIR spectra.

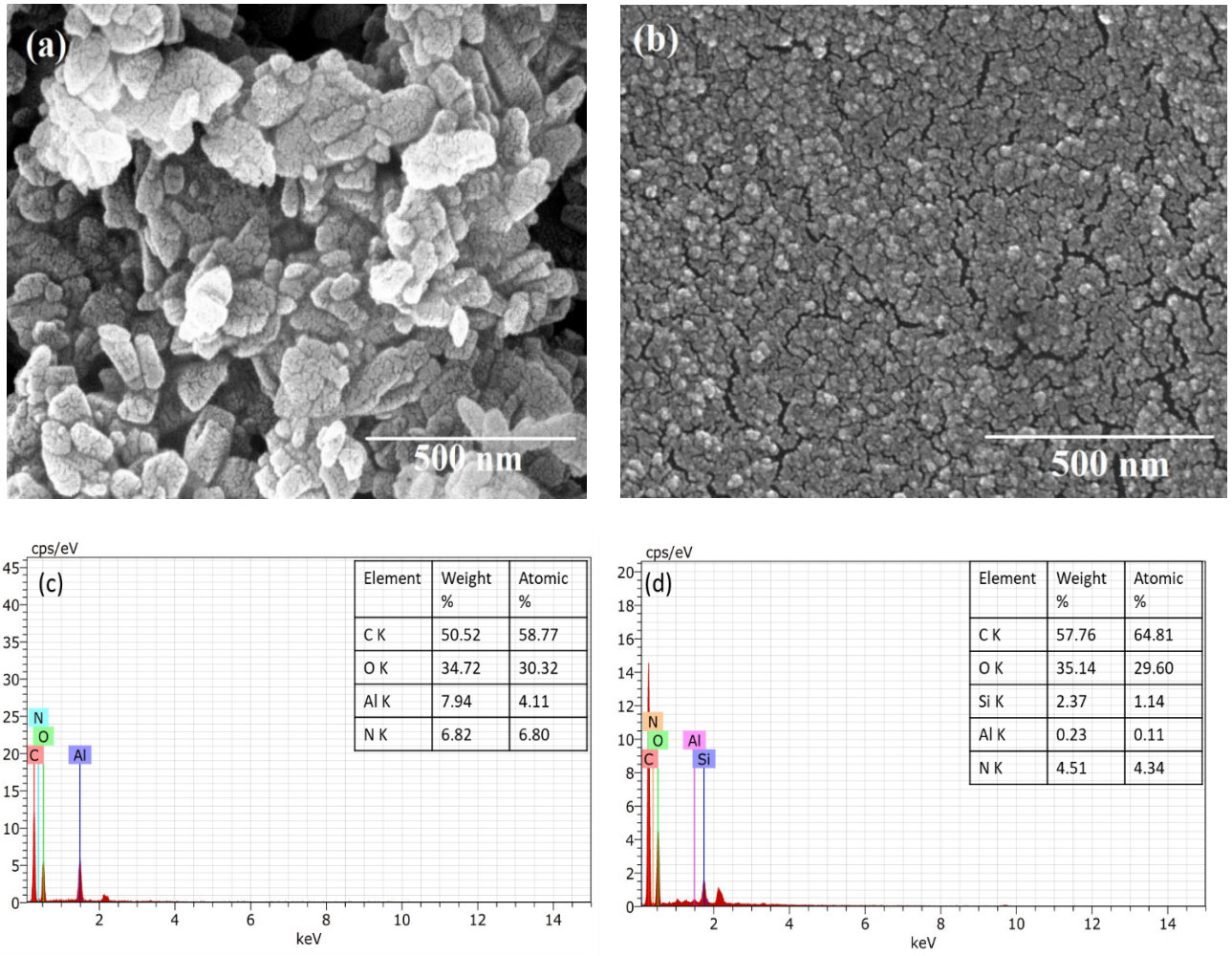

Figure 3. FE-SEM images and EDX spectra of (**a**,**c**) NH_2-MIL-53(Al) and (**b**,**d**) NH_2-MIL-53(Al)/MIP, respectively.

The effect of concentration of ciprofloxacin on fluorescence properties of Al-based MOF and its composite with MIPs is shown in Figure 4. Here, it is clear that there is no significant change in fluorescence properties of NH_2-MIL-53(Al) at lower (100 μM) and higher concentration (1000 μM) of ciprofloxacin, refer to curve a and b, respectively. However, a significant change in fluorescence of NH_2-MIL-53(Al)/MIP can be observed with increasing concentration of ciprofloxacin. As the concentration of ciprofloxacin increases form 100 μM to 1000 μM, a significant increase in fluorescence emission at 430 nm was observed with excitation 330 nm (refer to curve c and d, respectively). This significant change in fluorescence emission of the composite can be potentially utilized for detection of ciprofloxacin.

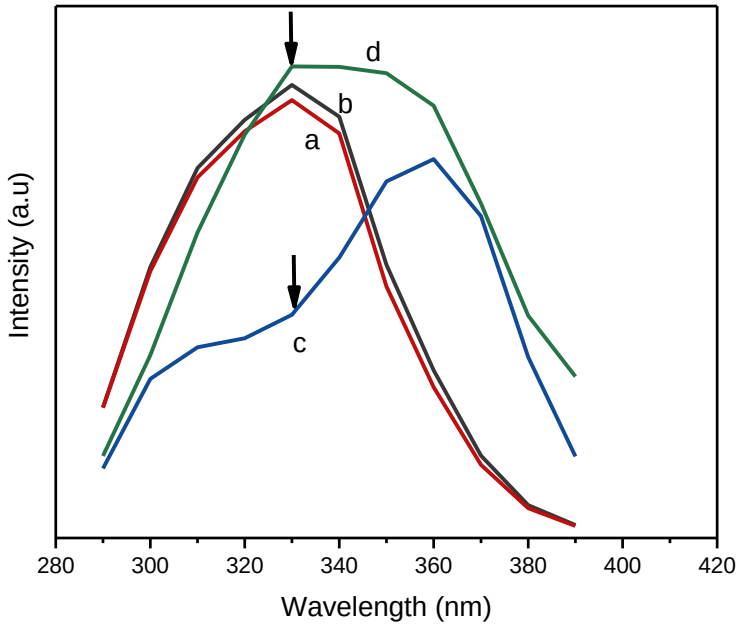

Figure 4. Optical characteristics of NH_2-MIL-53(Al) and NH_2-MIL-53(Al)/MIP in the presence of different concentrations of ciprofloxacin where a & b denote NH_2-MIL-53(Al) and c & d denote NH_2-MIL-53(Al) in the presence of increasing concentration of ciprofloxacin (100 μM and 1000 μM, respectively).

4. Conclusion

Nowadays, the screening of antibiotics is of utmost importance for safety of ecosystem and human health. Here, the synthesis of fluorescent NH_2-MIL-53(Al) was carried out using a hydrothermal approach. After confirmation of its crystalline nature and high surface area, its composite with MIP was developed via sol-gel approach. Ciprofloxacin-specific MIP has a significant impact over optical properties of NH_2-MIL-53(Al), i.e., UV-vis absorbance and fluorescence properties. The significant change in fluorescence emission from NH_2-MIL-53(Al)/MIP (at 430 nm with excitation at 330 nm) with increasing concentration of ciprofloxacin can be effectively utilized for its detection.

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Conflicts of Interest: The authors declare no conflict of interest.

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