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Abstract

Metal-organic frameworks (MOFs) are promising pharmaceutical adsorbents owing to their high porosity, tunable chemistry, and accessible metal sites. Here, copper-trimesate (Cu-BTC/HKUST-1) and iron-trimesate (MIL-100(Fe)) were synthesised by room-temperature co-precipitation and characterised using FTIR, XRD, FESEM, EDS, DLS, and zeta-potential analysis. Entrapment efficiency (EE%) of ibuprofen (IBU), ciprofloxacin (CIP), and paracetamol (PARA) was evaluated at MOF concentrations of 0–100 $\mu\text{g mL}^{-1}$ in anhydrous acetonitrile, pH 5.0, and pH 7.0 buffers for 24 h at 37 °C. Adsorption behaviour was assessed using pseudo-first-order, pseudo-second-order (PSO), Weber-Morris intraparticle diffusion, and Langmuir models. In acetonitrile, both MOFs achieved $\geq 97\%$ EE for all drugs at $\geq 25 \mu\text{g mL}^{-1}$, with PSO showing the best fit ($R^2 = 0.985\text{--}1.000$), indicating chemisorption. Langmuir analysis showed the capacity order $\text{CIP} > \text{IBU} > \text{PARA}$. Under aqueous conditions, adsorption was strongly pH-dependent: IBU showed maximum EE at pH 7.0, CIP maintained 81–83% saturation, and PARA exhibited a pH-independent anti-Langmuir response. MIL-100(Fe) showed superior CIP stability, whereas Cu-BTC enabled faster IBU adsorption. HPLC-DAD spike-recovery analysis in river water confirmed field-relevant applicability, with 90–95% recoveries and $\text{RSD} < 3.5\%$ for CIP, PARA, and IBU. These findings support MOF selection for pharmaceutical wastewater remediation.

Keywords: metal-organic frameworks; Cu-BTC; MIL-100(Fe); entrapment efficiency; pH-dependent adsorption.

1. Introduction

The increasing presence of pharmaceuticals in the aquatic environment has posed an increasing threat to the environment. Pharmaceuticals and personal care products (PPCPs) get discharged through hospitals' sewage and wastewater treatment plant (WWTP) effluents and agrochemical run-offs. Although treatments like coagulation, chlorination, and biological oxidation eliminate some of the drug substances, however many persistent compounds are not completely eliminated and remain in the water bodies (Luo et al., 2024; Rodriguez-Narvaez et al., 2017). The most common PPCPs include non-steroidal anti-inflammatory drugs (NSAIDs), fluoroquinolone antibiotics and analgesic antipyretics. Their effective removal requires selective adsorbents capable of targeting multiple pollutants (Kümmerer, 2010; Verlicchi et al., 2012).

Ibuprofen (IBU), an over-the-counter non-steroidal anti-inflammatory drug, exists in WWTP effluents in concentrations ranging from 0.1 to 10 $\mu\text{g L}^{-1}$ and as high as 168 $\mu\text{g L}^{-1}$ in surface water (Heberer, 2002). Ciprofloxacin (CIP), a fluoroquinolone antibacterial antibiotic with wide spectrum activity, has emerged as significant concern due to its contribution to promote the proliferation of antibiotic resistance genes even at sub-inhibitory concentrations, existing in concentrations of up to 124 $\mu\text{g L}^{-1}$ in hospital effluents and greater than 6 $\mu\text{g L}^{-1}$ in Indian rivers, highlighting its environmental impact (Fick et al., 2009; Larsson et al., 2007). Paracetamol (PARA; acetaminophen), another commonly used analgesic antipyretic, is present in highly concentrated amounts of up to 1,200 $\mu\text{g L}^{-1}$ in untreated hospital effluents and is poorly removed by WWTPs (Peralta-Hernández & Brillas, 2023).

Metal-organic frameworks (MOFs) have gained considerable attention from researchers as novel porous adsorbent materials due to their exceptionally large specific surface areas (500-7,000 $\text{m}^2 \text{g}^{-1}$), customizable porosity, and numerous open metal sites that provide suitable Lewis acidic centres for the adsorption of drug molecules (Furukawa et al., 2013; Horcajada et al., 2012). Compared to conventional adsorbents such as activated carbon and zeolites, MOFs exhibit better tunability in pore diameter, functionalization on the surface, and metal nodes architecture enabling formation of tailored adsorption systems for efficient removal of drug molecules (Khan et al., 2013). Some of the most investigated carboxylate-linked MOFs for elimination of pharmaceuticals include Cu-BTC (HKUST-1), which features a face-centered cubic type pore network containing both 9 Å and 5 Å windows, along with Cu^{2+} paddlewheel secondary building units (Chui et al., 1999), as well as MIL-100(Fe) (iron trimesate), which contains big mesoporous cages of 29 and 34 Å along with Fe^{3+} trimers as secondary building

units (Férey et al., 2005). As both frameworks contain same trimesic acid (BTC) linker, they provide an ideal platform, for direct comparisons of how the Cu^{2+} and Fe^{3+} metals affect adsorption and uptake capacity of pharmaceutical compounds.

Although significant progress has been achieved concerning the use of MOFs for pharmaceutical adsorption, many questions regarding mechanisms are still unresolved. The vast majority of research is conducted for single pharmaceutical compound with a specific solvent, often neglecting the influence of pH-dependent drug ionization on drug- MOF interactions a shift from physisorption to chemisorption of MOF-metal nodes (Dias & Petit, 2015; Hasan & Jung, 2015). Kinetics studies frequently use pseudo-first and second order equations with no validation and thus cannot clearly show real rate-limiting steps (Simonin, 2016). Mass transfer processes such as film diffusion, which determines the intraparticle diffusion into pore structures, is not often considered in conjunction with chemisorption on surfaces (Wu et al., 2009). The multi-drug studies which include diverse types of interactions (coordinate, hydrogen bonds, and physisorption) are scarce, hence limiting the development of broadly applicable absorption models (Bhadra et al., 2016). Furthermore, comparisons across different studies become difficult because of the differences in various parameters like drug concentration, amount of adsorbent, contact time etc which complicate the establishment of standardized performance benchmarks (Foo & Hameed, 2010).

The present study systematically investigated the adsorption behaviour of ibuprofen (IBU), ciprofloxacin (CIP), and paracetamol (PARA) in two BTC-based metal-organic frameworks, Cu-BTC and MIL-100(Fe), under non-aqueous and aqueous conditions. Specifically, the study aimed to quantify the adsorption capacity and affinity of each drug-MOF system by determining the Langmuir adsorption parameters, namely the maximum encapsulation efficiency (EE_{max}) and equilibrium binding constant (K^d). Furthermore, adsorption kinetics were evaluated to distinguish physisorption from chemisorption using pseudo-first-order (PFO) and pseudo-second order (PSO) kinetic models, while the Weber-Morris intraparticle diffusion (IPD) model was employed to identify the rate-limiting diffusion processes. The influence of drug ionization on adsorption behaviour was assessed by comparing adsorption characteristics in acetonitrile (ACN), pH-adjusted aqueous solution at pH 5.0, and pH-adjusted aqueous solution at pH 7.0. Collectively, these investigations establish a mechanistic framework describing MOF-drug interactions across different adsorption environments and provide design principles for developing MOF-based adsorbents for pharmaceutical wastewater remediation.

2. Materials and Methods

2.1 Chemicals and Reagents

All reagents were of analytical grade and were not subjected to any further purification. Copper (II) nitrate trihydrate, trimesic acid (BTC), ferrous sulfate heptahydrate, sodium hydroxide, ibuprofen (IBU), ciprofloxacin (CIP), paracetamol (PARA), sodium phosphate, and other analytical reagents were supplied by Sisco Research Laboratories (SRL), Mumbai, India. N,N-dimethylformamide (DMF), dichloromethane (DCM), absolute ethanol, and acetonitrile of HPLC grade were supplied by Merck India Ltd., Mumbai, India. Solutions of pH 5.0 and pH 7.0 were prepared for the study of adsorption, and deionized water (18 M Ω ·cm) was prepared using a Milli-Q purification system.

2.2 Experimental Design

Adsorption of IBU, CIP, and PARA on Cu-BTC and MIL-100(Fe) was investigated under non-aqueous and aqueous conditions. The study involved MOF preparation and characterisation, adsorption experiments in anhydrous acetonitrile (ACN), pH 5.0 and pH 7.0, followed by equilibrium and kinetic modelling. ACN was first used to evaluate intrinsic drug-MOF interactions before assessing pH-dependent adsorption in aqueous media. Drug solutions (1 mg mL⁻¹) were treated with 0-100 μ g mL⁻¹ MOF for 24 h and quantified by UV-Vis; this higher concentration ensured reliable quantification and systematic assessment of adsorption, while μ g L⁻¹ concentrations were used for river-water analysis to represent environmentally relevant levels. Equilibrium and kinetic behaviour were evaluated using Langmuir, pseudo-first-order (PFO), pseudo-second-order (PSO), and Weber-Morris intraparticle diffusion (IPD) models. The selected pH values represent mildly acidic and near-neutral conditions relevant to pharmaceutical manufacturing wastewater. Method applicability was further assessed in Mula-Mutha River water collected from Pune, India (18°32.206' N, 73°56.015' E) using HPLC-DAD as a field-relevant validation (Kümmerer, 2010).

2.3 Synthesis of Metal-Organic Frameworks

2.3.1 Synthesis of Cu-BTC (HKUST-1)

The Cu-BTC complex was synthesized via co-precipitation at room temperature. BTC at concentration 19.8 mg mL⁻¹ and Cu(NO₃)₂·3H₂O at concentration 34.2 mg mL⁻¹ were individually dissolved in DMF/EtOH/H₂O (1:1:1) solvent mixture and then combined with stirring for 2 to 3 h at room temperature to form blue crystalline precipitates (Liu et al., 2025) obtained product was filtered using vacuum filtration method and then washed using DMF and further subjected to solvent change using dichloromethane (three times in 24 h) to eliminate

DMF. Lastly, it was activated under high vacuum (≤ 5 mTorr) to get blue-violet Cu-BTC powder.

2.3.2 Synthesis of MIL-100(Fe)

The preparation of MIL-100(Fe) was done using an aqueous co-precipitation technique. BTC (26.3 mg mL^{-1}) and NaOH (15.0 mg mL^{-1}) were dissolved in deionised water to form Solution A, whereas $\text{FeSO}_4 \cdot 7\text{H}_2\text{O}$ (50.8 mg mL^{-1}) was dissolved in deionised water to form Solution B. Solution A was gradually added to Solution B while stirring magnetically (150 rpm) for 1 h at room temperature, giving rise to a light orange precipitate. The precipitate was purified by centrifugation, washed with deionised water to eliminate any traces of the remaining chemicals and dried to get MIL-100(Fe) (L. Lu et al., 2025).

2.4 Physicochemical Characterisation

The synthesised MOFs were characterised by FTIR (SHIMADZU IRSpirit-L, ATR mode, $400\text{--}4000 \text{ cm}^{-1}$), XRD (Rigaku MiniFlex 300/600, Cu K α , $\lambda = 1.5406 \text{ \AA}$; $2\theta = 3\text{--}90^\circ$), FESEM, and EDS (TESCAN CLARA with Oxford Instruments detector). Particle size distribution and zeta potential were determined using a Malvern Panalytical Zetasizer Lab Blue. All measurements were performed in triplicate ($n = 3$) and reported as mean $\pm$ SD.

2.5 UV-Vis Calibration and Drug Quantification

Concentrations of the drugs were determined with a BioTek Synergy H1 Hybrid Multi-Mode Microplate Reader with calibration plots ($0\text{--}100 \text{ }\mu\text{g mL}^{-1}$) made for every solvent system used. Wavelengths of analysis in acetonitrile solution were 222 nm (IBU), 277 nm (CIP), and 243 nm (PARA), and 264 nm, 350 nm, and 295 nm (aqueous buffers) accordingly. Beer-Lambert linear regression ($20\text{--}100 \text{ }\mu\text{g mL}^{-1}$) was used for concentration determination. Real river water samples were additionally analysed using an HPLC-DAD system for cross-validation under field-matrix conditions (Section 2.9).

Net absorbance was calculated using Equation (1):

$$A_{\text{net}} = A_{\text{sample}} - A_{\text{MOF-control}} - A_{\text{blank}}$$

where A_{sample} is the absorbance of the drug-loaded MOF suspension, $A_{\text{MOF-control}}$ is the absorbance of the corresponding MOF suspension without drug, and A_{blank} is the solvent or buffer absorbance. Corrected absorbance values were converted to drug concentrations using the respective calibration curves (Kiteto & Mecha, 2024).

2.6 Entrapment Efficiency and Kinetic Studies

Loading test for the drugs was performed in 96-well microplate at 37°C by linear shaking continuously. MOFs solution was prepared in concentration of $0\text{--}100 \text{ }\mu\text{g mL}^{-1}$ in three solvent

systems. The Entrapment Efficiency (EE%) was tested hourly for 24 hours. The formula to calculate EE% is:

$$EE (\%) = [(C_0 - C_s) / C_0] \times 100$$

where C_0 was the initial drug concentration (1000 $\mu\text{g mL}^{-1}$) and C_s concentration of untrapped drug in the supernatant after the incubation with MOFs (Horcajada et al., 2012).

2.7 Adsorption Kinetic Modelling

Adsorption kinetics were analysed using the pseudo-first-order (PFO), pseudo-second-order (PSO), and Weber-Morris intraparticle diffusion (IPD) models. The PFO model was expressed as:

$$q_t = q_e(1 - e^{-k_1 t})$$

where q_t and q_e are the adsorption capacities at time t and equilibrium, respectively, and k_1 is the rate constant (Simonin, 2016). The PSO model was evaluated using:

$$\frac{t}{q_t} = \frac{1}{k_2 q_e^2} + \frac{t}{q_e}$$

where k_2 is the pseudo-second-order rate constant (Ho & McKay, 1999). Intraparticle diffusion was assessed using the Weber-Morris model:

$$q_t = k_{id} t^{0.5} + C$$

where k_{id} is the diffusion rate constant and C represents the boundary layer effect. Model suitability was assessed using the coefficient of determination (R^2) and agreement between calculated and experimental adsorption capacities (Weber & Morris, 1963).

The dose-response relationship was analysed using the Langmuir saturation model:

$$EE(\%) = \frac{EE_{\max} \times [MOF]}{K_d + [MOF]}$$

where $EE_{\max}$ is the maximum entrapment efficiency, K_d is the apparent dissociation constant, and $[MOF]$ is the MOF concentration.

2.8 Post-Loading Characterisation

Drug-loaded MOF composite particles were collected by centrifugation (10,000 $\times g$, 10 min), followed by washing with fresh solvent twice and drying under vacuum at 40°C for 24 hours. FTIR spectra of the drug-loaded composites were compared with that of pristine MOFs as well as with the spectrum of the pure drug molecules to identify MOF-drug interactions and bond formation.

2.9 HPLC-DAD Analysis

HPLC-DAD analysis was performed using an LC-20AT pump equipped with an SPD-M20A diode-array detector, SIL-20A HT autosampler, and CTO-10AS VP column oven (Shimadzu,

Kyoto, Japan). Chromatographic separation was carried out on a Hypersil Gold C18 reverse-phase column (250×4.6 mm, $5 \mu\text{m}$; Thermo Scientific, Waltham, MA, USA) using acidified water (1% acetic acid)/acetonitrile (50:50, v/v) as the mobile phase at a flow rate of 1.0 mL min^{-1} . The column temperature was maintained at 40°C , with an injection volume of $10 \mu\text{L}$. DAD detection was performed at 295 nm for paracetamol (PARA), 350 nm for ciprofloxacin (CIP), and 264 nm for ibuprofen (IBU). The method was applied for chromatographic identification and quantification of the target pharmaceuticals in river-water samples (Syed Yaacob et al., 2018).

3. Results and Discussion

3.1 Synthesis and Physicochemical Characteristics of MOFs

Cu-BTC (HKUST-1) and MIL-100(Fe) were successfully synthesized using room-temperature co-precipitation methods as described in Section 2.2. Cu-BTC was obtained as a blue-violet crystalline powder with an overall yield of 58.3%, whereas MIL-100(Fe) was obtained as a light orange powder with an approximate yield of 74.9%. The higher yield of MIL-100(Fe) suggests more efficient framework formation under the employed aqueous synthesis conditions. The successful formation of both MOFs was further confirmed by XRD, FTIR, SEM, and zeta potential measurements.

3.1.1 FTIR Spectroscopy

The FTIR spectra of both the MOFs exhibited distinctive absorption peaks in the range $1624\text{--}1404 \text{ cm}^{-1}$, which can be attributed to the asymmetric and symmetric vibrations of the coordinating ($-\text{COO}-$) group (Prestipino et al., 2006; Serre et al., 2007) (Figure 1). Additional absorption peaks were observed in the range $760\text{--}457 \text{ cm}^{-1}$ which could be attributed to metal-oxygen vibrations and ring deformations. Notably, the lack of major peaks corresponding to free carboxylic acid groups, especially a broad O-H stretch in the range $2500\text{--}3300 \text{ cm}^{-1}$ and a sharp C=O stretching peak around 1700 cm^{-1} , indicates successful incorporation of BTC ligands in both structures (Tranchemontagne et al., 2009). FTIR studies performed on drug-loaded Cu-BTC and MIL-100(Fe) showed additional peaks or shifts in the spectra in comparison with MOF without drug molecules, suggesting that the absorption occurred through multiple intermolecular interactions including coordinate bonding, hydrogen bonding, and π -stacking interactions between the aromatic rings of the drug molecules and the organic linkers of the MOFs (Figure 6).

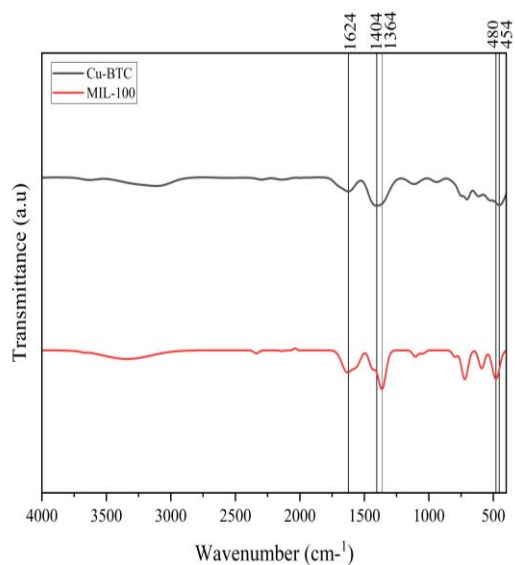


Figure 1 FTIR spectrum Cu-BTC and MIL-100, recorded using Shimadzu IRSpirit- L at a range of 4000-400 cm⁻¹.

3.1.2 XRD Analysis

XRD analysis confirmed the successful formation of highly crystalline Cu-BTC and MIL-100(Fe) frameworks (Figure 2). Cu-BTC displayed characteristic diffraction peaks at $2\theta = 6.7^\circ$, 9.5° , 11.6° , 13.4° , and 17.4° , consistent with the HKUST-1 face-centred cubic structure (Fm-3m) (Férey et al., 2005; Prestipino et al., 2006). MIL-100(Fe) displayed the typical broad diffraction pattern of Fd-3m phase without any additional crystalline phases (Hasan & Jhung, 2015). These diffraction patterns are consistent with previously published results, confirming the validity of the synthesis techniques employed in this study (Alaerts et al., 2006; Jhung et al., 2007).

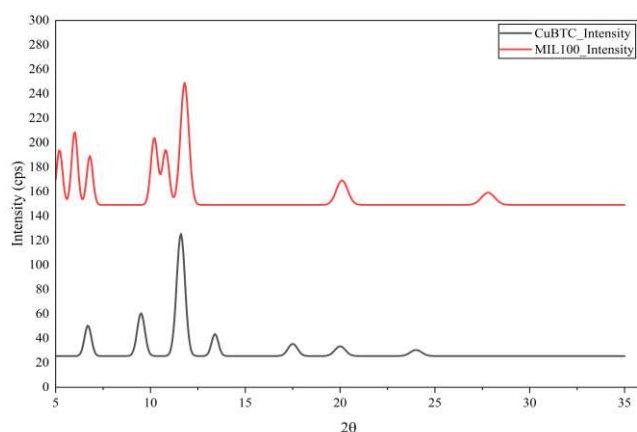


Figure 2 Powder X-ray diffraction (XRD) patterns of synthesized Cu-BTC and MIL-100 metal-organic frameworks, confirming their crystalline structures.

3.1.3 FESEM and EDS Analysis

FESEM results showed distinct morphological features. The Cu-BTC sample showed defined octahedral or polyhedral morphology with clear faces, suggesting controlled nucleation and crystal growth processes in agreement with the morphologies of HKUST-1 described in literature (Chui et al., 1999). The MIL-100(Fe) framework had a highly aggregated morphology comprising of interlinked spherical nanoparticles with a porous cluster structure, which allowed easy mass transport within the framework (Figure 3) (Qian et al., 2012). EDS analysis confirmed elemental compositions of C, O, and Cu for Cu-BTC and C, O, and Fe for MIL-100(Fe), with no significant impurity peaks, corroborating XRD phase purity (Figure 4).

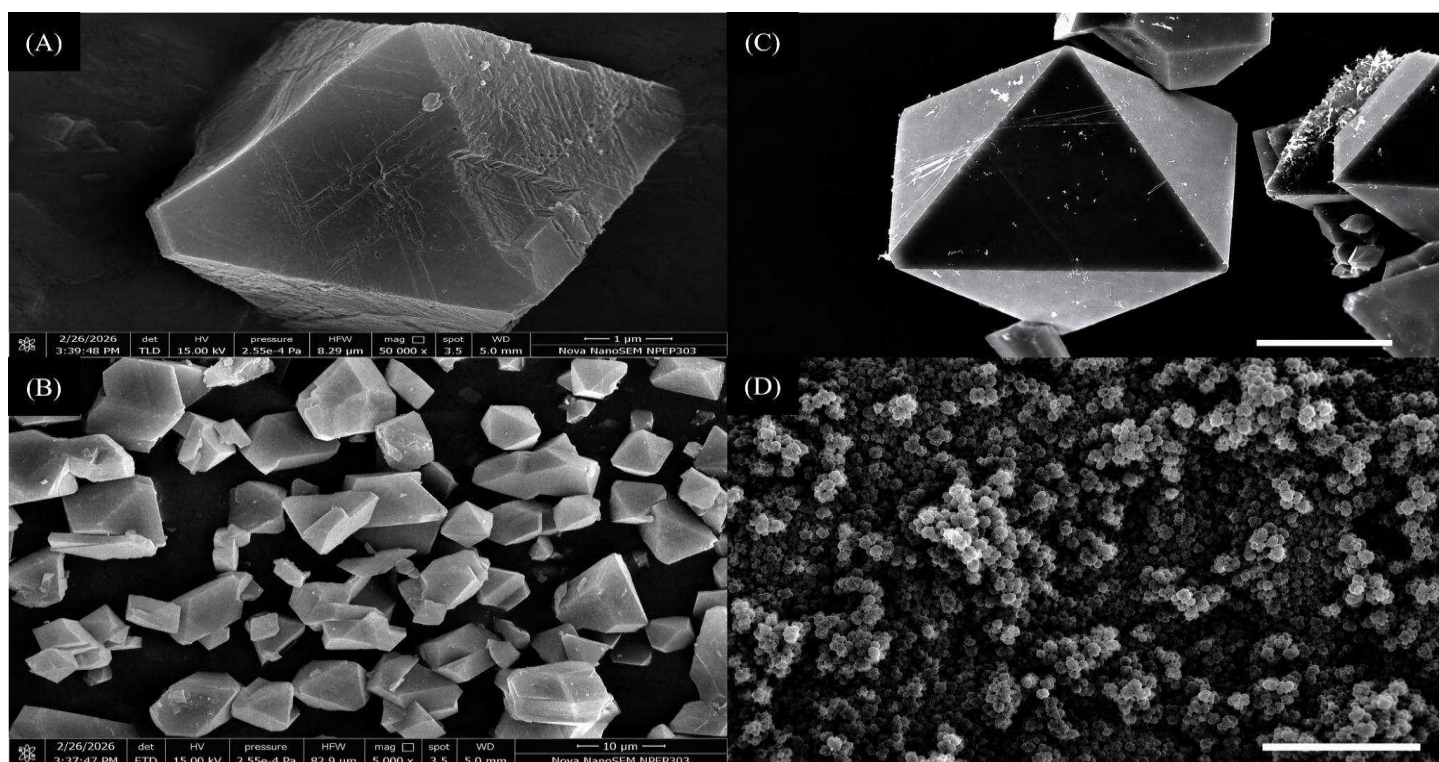


Figure 3 FE- SEM micrographs of Cu-BTC at (A) 1 μm , (B) 10 μm , and MIL-100 (C) 1 μm , and (D) 10 μm magnifications.

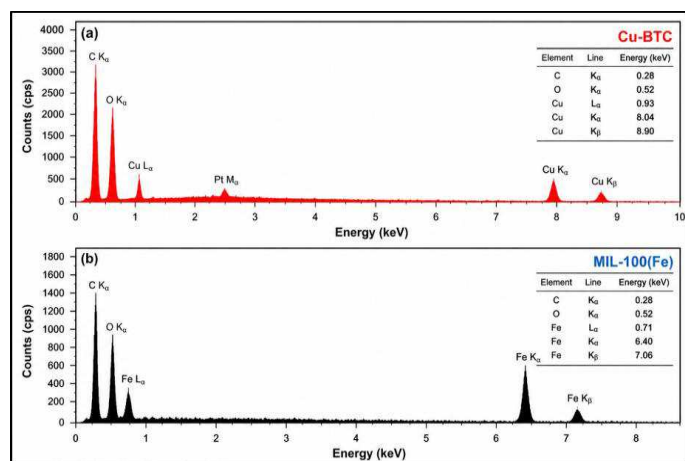


Figure 4 EDS plot of (a) Cu-BTC and (b) MIL-100(Fe) to confirm yield and synthesis of MOFs.

3.1.4 DLS and Zeta Potential

The obtained results show similarity to the sizes of Cu-BTC (70 nm) and MIL-100(Fe) (90 nm) nanoparticles synthesized earlier, confirming the effectiveness of the synthesis and the availability of a large external surface area and diffusion distance favourable for adsorption reactions (Cai et al., 2019; Wuttke et al., 2015). Zeta potential measurements showed both MOFs were negatively charged (Cu-BTC: -45 mV; MIL-100(Fe): -38 mV), indicating good colloidal stability. Cu-BTC should exhibit a higher degree of negative surface charge and thus facilitate electrostatic interaction with the positively charged ciprofloxacin at pH 5.0. The recorded zeta potential values range from -30 mV to -50 mV and align with the literature values, supporting the suitability of both MOFs for pharmaceutical adsorption (Rojas et al., 2016).

3.1.5 Post-Loading Characterisation

The FTIR spectra of drug-impregnated Cu-BTC and MIL-100 (Figure 5), confirmed that CIP, IBU, and PARA drugs have been successfully encapsulated in the MOFs. Characteristic bands belonging to the MOF frameworks remained intact upon encapsulation. However, minor shifts, band broadening, and intensity changes were observed in the 1700-1200 cm^{-1} region, along with broadening of the O-H/N-H stretching vibrations in 3600-3000 cm^{-1} range. This suggests existence of intermolecular interactions between the drug molecules and the MOF frameworks. The lack of significant spectral changes or the presence of framework peaks suggests that the drug integration took place through non-covalent host-guest interaction without affecting the structure of the MOF.

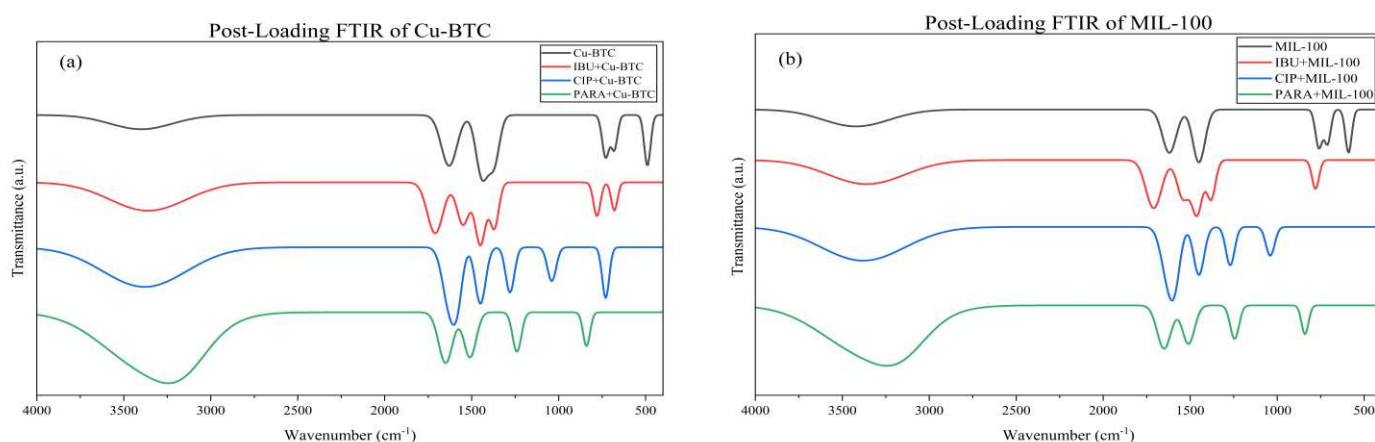


Figure 5 FTIR spectra of drug-loaded (a) Cu-BTC and (b) MIL-100 following encapsulation of ciprofloxacin (CIP), ibuprofen (IBU), and paracetamol (PARA).

3.2 Acetonitrile Kinetic Study and Model Fitting

3.2.1 Calibration Curves in Acetonitrile

Calibration plots have been made in anhydrous acetonitrile at wavelengths of 222 nm (IBU), 277 nm (CIP), and 243 nm (PARA), which represent their individual maxima for UV absorption (Chan et al., 2004). The determination of drug levels was done using Beer-Lambert law from a concentration of 20-100 $\mu\text{g mL}^{-1}$. The linearity of IBU and CIP was found to be relatively low due to the fact that acetonitrile is not a protic solvent (Reichardt & Welton, 2010), whereas PARA showed a stronger linear response ($R^2 = 0.761$) due to its well-defined amide-phenol chromophore.

3.2.2 Dose-Dependent Entrapment Efficiency in Acetonitrile

In anhydrous acetonitrile, both MOFs demonstrated fast and efficient adsorption properties, with significant EE% enhancements in MOFs at 5 $\mu\text{g mL}^{-1}$ concentration (Figure 6). Complete encapsulation was obtained for CIP and PARA in both MOFs (100%), while IBU reached 99.1% EE in Cu-BTC and 100% at MOF concentrations $\geq 25 \mu\text{g mL}^{-1}$. The observed plateau is consistent with Langmuir-type saturation, where available adsorption sites become fully occupied (Horcajada et al., 2012; C.-Y. Sun et al., 2013). A temporary drop in IBU/Cu-BTC EE% at 75 $\mu\text{g mL}^{-1}$ (0 h) was associated with experimental variation since full adsorption was achieved at 24 h. On the other hand, adsorption of CIP in Cu-BTC decreased at 6 h at higher amounts of MOFs (50-100 $\mu\text{g mL}^{-1}$) because of the competition from acetonitrile solvation, while MIL-100(Fe) exhibited higher adsorption due to its more developed pores and strong Fe^{3+} -fluoroquinolone interaction as documented earlier (W. Lu et al., 2014; C.-Y. Sun et al., 2013).

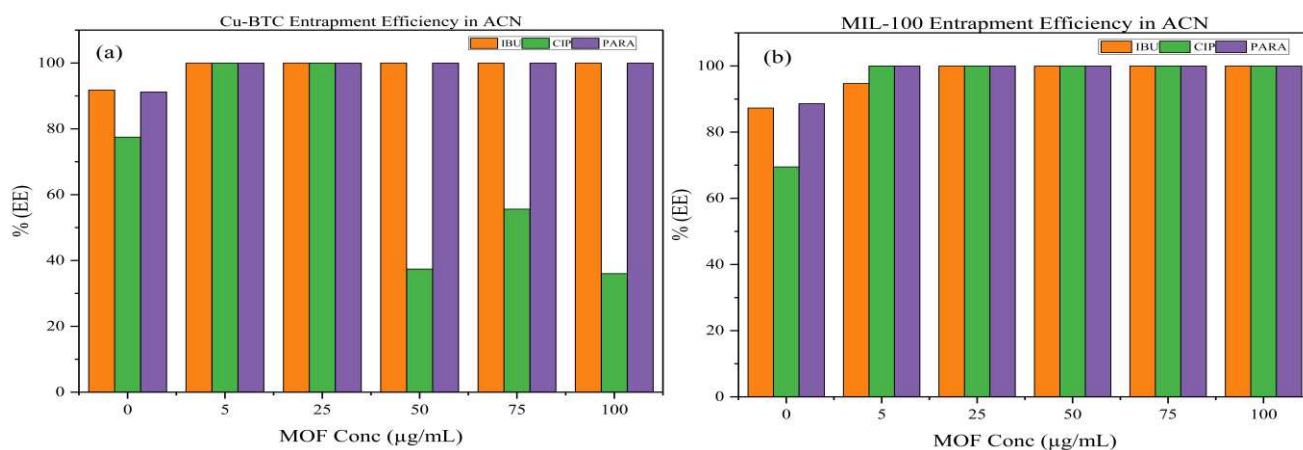


Figure 6 Effect of MOF concentration on the entrapment efficiency (EE%) of ibuprofen, ciprofloxacin, and paracetamol in acetonitrile. (a) Cu-BTC and (b) MIL-100(Fe) was

investigated at concentrations of 0, 5, 25, 50, 75, and 100 $\mu\text{g mL}^{-1}$ to assess their drug loading performance.

3.2.3 PSO and PFO Kinetic Analysis in Acetonitrile

However, Pseudo-first order model was not appropriate for all systems since adsorption was already at equilibrium before the first sampling. The lone exception to this was the IBU/Cu-BTC system with 75 $\mu\text{g mL}^{-1}$ concentration where the PFO model had low correlation coefficient ($R^2 = 0.426\text{-}0.534$) as compared to the acceptance criteria ($R^2 \geq 0.99$) (Ho & McKay, 1999). On the other hand, the pseudo-second-order (PSO) kinetic equation demonstrated high correlation to all the drug-MOF systems ($R^2 = 0.985\text{-}1.000$) and predicted their equilibrium binding capacities in close agreement with the actual data. The PSO constants for IBU binding to MIL-100(Fe) were higher compared to Cu-BTC, suggesting more rapid metal coordination with Fe^{3+} sites, consistent with previous reports (Foo & Hameed, 2010; Wei et al., 2014). CIP adsorption on both the MOFs gave PSO kinetics with near-perfect correlation ($R^2 = 1.000$), which indicates rapid bidentate binding of the fluoroquinolone to the metal sites (Taylor-Pashow et al., 2009). PSO was also obtained for PARA adsorption ($R^2 = 0.987\text{-}1.000$), indicating the dominance of hydrogen bonding and pore interactions (Langmuir, 1918). In general, the perfect PSO behavior and the poor PFO behavior clearly show that the chemisorption mechanism controls the rate of the process in all systems studied.

3.2.4 Weber-Morris Intraparticle Diffusion in Acetonitrile

Weber-Morris IPD model was only used in those systems where there were observable heterogeneous kinetics. IBU-Cu-BTC system at 75 $\mu\text{g mL}^{-1}$ concentration showed the best correlation ($R^2 = 0.899$). Non-zero intercept suggests that both film diffusion and intraparticle diffusion contribute to the adsorption process due to hierarchical porosity of HKUST-1 (Weber & Morris, 1963). The results from CIP showed quick equilibrium at low concentrations of MOF, and thus IPD modeling could not be applied, but at high Cu-BTC concentrations, there was a negative slope for diffusion, indicating desorption or adsorbate rearrangement rather than true intraparticle diffusion (Huang et al., 2020). The diffusion coefficient was found to be very low ($k_{id} = 0.088\text{-}0.095 \text{ mg g}^{-1} \text{ h}^{-0.5}$), for PARA, indicating adsorption through hydrogen bonds. In summary, the applicability of IPD model to the limited extent and the existence of non-zero intercepts confirm that adsorption is controlled by several mass transfer mechanisms including film diffusion, surface interactions, and intraparticle diffusion.

3.2.5 Langmuir Dose-Response Analysis in Acetonitrile

Langmuir analysis of equilibrium entrapment efficiency (EE%) predicted maximum adsorption capacities (EE_{max}) of 82%, 72%, and 58% for CIP, IBU, and PARA, respectively, with

corresponding K_d values of 15, 18, and 25 $\mu\text{g mL}^{-1}$ (Figure 7). The Cu-BTC and MIL-100(Fe) compounds exhibited great fits of Langmuir equation ($R^2 = 1.000$), suggesting that equilibrium adsorption capacity is dependent on the chemical nature of the drug molecules' functional groups rather than the metal nodes. The capacity of adsorption was in the order $\text{CIP} > \text{IBU} > \text{PARA}$ due to bidentate complexation, monodentate carboxylate coordination, and hydrogen bonding interactions (Deng et al., 2012; Peng et al., 2013). Even though experimental EE% reached 100% in acetonitrile solvent, the Langmuir-calculated lower EE_{max} is most likely due to the fact that adsorption in aqueous environment suffers from solvent competition.

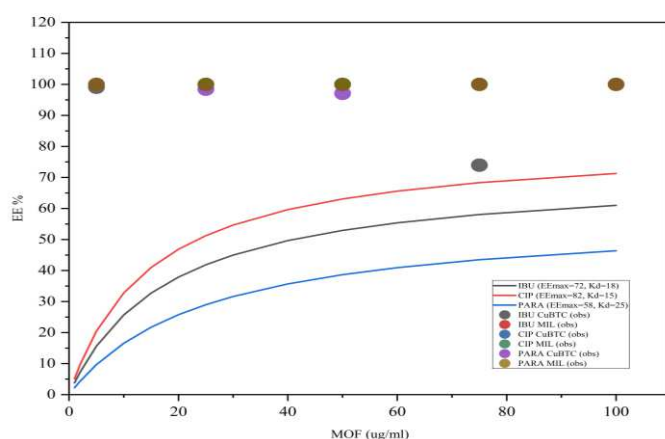


Figure 7 Langmuir dose-response curves for CIP, IBU, and PARA entrapment in acetonitrile. Solid lines represent Langmuir fits, while symbols indicate experimental EE% values for Cu-BTC and MIL-100(Fe).

3.3 pH-Dependent Kinetic Study at pH 5.0 and pH 7.0

In accordance with results from the acetonitrile dose-response experiment (Section 3.2.2), MOF concentrations ranging between 5 and 75 $\mu\text{g mL}^{-1}$ were chosen for pH aqueous tests because of their maximal drug loading efficiency. The highest 100 $\mu\text{g mL}^{-1}$ dose was not used due to the formation of aggregated sediments in the buffer, thus causing imprecise calculation of EE%, as a result of the instability of carboxylate MOFs in aqueous buffers (Wuttke et al., 2015).

3.3.1 Calibration Curves at pH 5.0 and pH 7.0

Calibration curves in the aqueous buffer solution medium in pH 5.0 and pH 7.0 were highly linear ($R^2 = 1.000$) in the selected wavelengths for the analysis (264 nm for IBU; 350 nm for CIP; 295 nm for PARA). The use of the secondary maximum of absorption of CIP at 350 nm instead of 271 nm was required to prevent detector saturation. Slight bathochromic shift of about 2 nm was observed for CIP at pH 7.0 relative to pH 5.0 as a result of more intensive π -electron delocalisation in zwitterionic species. However, this had no impact on linearity and

accuracy of quantification at 350 nm (Dias & Petit, 2015). The reason for insensitivity of the parameters of calibration of IBU and PARA to the pH of the buffers used is that the two substances undergo transitions of their aromatic ring irrespective of the solvent used.

3.3.2 Entrapment Efficiency at pH 5.0

Under a pH of 5.0, ibuprofen ($pK_a = 4.9$) displayed a normal Langmuir-type dose response curve where the percentage efficiency (EE%) of Cu-BTC and MIL-100(Fe) MOFs increased from 88.1% to 100.0% and 84.1% to 98.5%, respectively (Figure 8). Moderate ionisation enabled adsorption through combined carboxylate-metal coordination and hydrogen bonding, consistent with previous reports (Navalón et al., 2023).

Ciprofloxacin, present predominantly in its cationic form ($pK_{a1} = 6.1$), showed nearly constant EE% (82-83%) across all MOF concentrations. This dose-independent plateau suggests rapid saturation of adsorption sites, with binding dominated by π - π stacking, hydrogen bonding, and limited coordination despite electrostatic repulsion, in agreement with earlier studies (Liang et al., 2015).

Paracetamol stayed inert ($pK_a = 9.5$) and adsorbed via hydrogen bonding and van der Waals forces. Cu-BTC showed anti-Langmuir behavior, where EE% decreased from 91.6% to 82.2% with increasing MOF concentration, presumably due to the solvent-MOF competition for the framework sites despite increased accessibility of pores.

3.3.3 Entrapment Efficiency at pH 7.0

At pH 7.0, ibuprofen had become completely deprotonated with maximized carboxylate binding with metal nodes in MOFs. Complete extraction efficiency of 100% was achieved for both Cu-BTC and MIL-100(Fe) at $75 \mu\text{g mL}^{-1}$, with MIL-100(Fe) retaining 92.7% EE at $50 \mu\text{g mL}^{-1}$ concentration (Figure 8). The increased extraction efficiency agrees with HSAB theory that deprotonated carboxylates have strong binding affinity towards Cu^{2+} and Fe^{3+} metal centers as previously reported for carboxylates containing pharmaceuticals in MOFs (Liédana et al., 2012; Lim & Lee, 2010; McKinlay et al., 2010).

Ciprofloxacin, mostly in form of zwitterion, showed little variation of EE% (80.6-83.1%) in comparison with pH 5.0, implying that the adsorption of the compound is controlled by more than one type of interaction, such as coordination, π - π stacking and van der Waals interactions, thus producing pH independent performance (Liang et al., 2015). This robustness is advantageous for pharmaceutical wastewater treatment across varying pH conditions.

Paracetamol remained largely neutral and showed similar EE% to that observed at pH 5.0 (Cu-BTC: 92.1-79.8%), confirming that its adsorption is dominated by hydrogen bonding and is largely insensitive to pH. Overall, the pH-dependent changes observed for IBU and CIP arise

primarily from differences in their ionisation states and consequent coordination with MOF metal centres, rather than from the buffer medium itself.

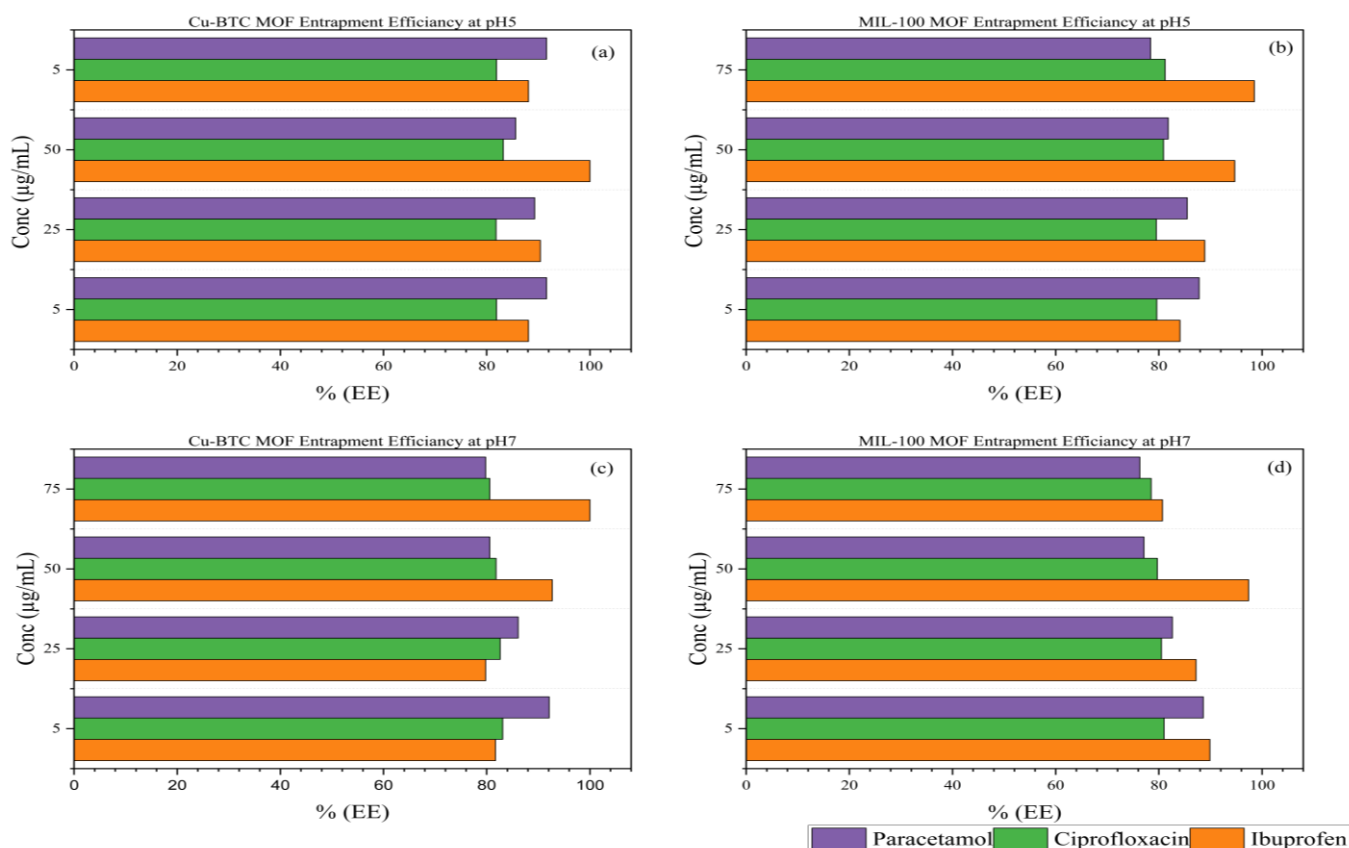


Figure 8 Entrapment efficiency (EE%) of ibuprofen, ciprofloxacin, and paracetamol in Cu-BTC and MIL-100 MOFs at pH 5.0 and pH 7.0. (a) Cu-BTC (pH 5.0), (b) MIL-100(Fe) (pH 5.0), (c) Cu-BTC (pH 7.0), and (d) MIL-100(Fe) (pH 7.0), evaluated at drug concentrations of 5, 25, 50, and 75 $\mu\text{g mL}^{-1}$.

3.3.4 Kinetic Release Profiles at pH 5.0 and pH 7.0 (0-24 h)

A biphasic release profile was observed in the case of ibuprofen loaded on Cu-BTC, which included an initial burst phase followed by slower release. This was the same for pH 5 and 7 conditions; however, the former witnessed a fall from 13.5% to 6.8% release within 24 hours while in the latter, the drop occurred from 22.4% to 8.8% release in just 6 hours (Horcajada et al., 2010). Release of ibuprofen from Cu-BTC at MOF concentrations $\geq 50 \mu\text{g mL}^{-1}$ was found to be negligible.

Release of ciprofloxacin was nearly constant (20-24%) in 24 hours for both pH values indicating a dynamic balance between adsorption and desorption of the drug. However, the marginal increase in the level of release due to high loading (75 $\mu\text{g mL}^{-1}$) was explained by competitive displacement from weaker sites.

Paracetamol showed moderate levels of release (8-30%) for both pH values owing to reversible hydrogen-bonded adsorption of the drug instead of irreversible chemisorption. However, the fall in the level of release (34.2% to 18.5%) for 24 hours at pH 7.0 indicated competitive adsorption of ionised species.

3.3.5 Kinetic Modelling at pH 5.0 and pH 7.0

Pseudo-first order (PFO) kinetics explained just 7.7% of the studied drug-MOF-pH systems (with $R^2 \geq 0.95$), and 57.7% had poor correlation ($R^2 < 0.70$), thus confirming that physisorption is not dominant adsorption mechanism. For the adsorption of IBU/MIL-100(Fe) in PFO, the optimal conditions were at pH 5.0 and 5 $\mu\text{g/mL}$ MOF concentration ($R^2 = 0.9824$). On the other hand, the adsorption of CIP showed very low R^2 values ($R^2 = 0.04-0.78$), confirming that its adsorption cannot be explained by simple physisorption (Gadipelly et al., 2018).

In contrast, the pseudo-second-order (PSO) model provided excellent fits for ibuprofen and the drug mixture ($R^2 \geq 0.99$), demonstrating that chemisorption governs adsorption. Increasing the pH from 5.0 to 7.0 markedly enhanced the PSO rate constant (k_2): for IBU-Cu-BTC, k_2 increased 4.5-fold and the initial adsorption rate increased 28-fold, while MIL-100(Fe) showed a nine-fold increase in k_2 . These improvements are attributed to complete carboxylate deprotonation, which promotes stronger coordination with Cu^{2+} and Fe^{3+} metal centres (Pearson, 1963). Overall, PSO consistently outperformed PFO, confirming chemisorption as the predominant adsorption mechanism, particularly under neutral conditions.

3.3.6 Weber-Morris IPD Analysis at pH 5.0 and pH 7.0

The highest influence of the pH on the IBU-Cu-BTC system was observed at a concentration of 5 $\mu\text{g mL}^{-1}$, where the intraparticle diffusion rate constant (k_{id}) changed by 1.71 times from 3.198 (at pH 5.0; $R^2 = 0.712$) to 5.463 $\text{mg g}^{-1} \text{h}^{-0.5}$ (pH 7.0; $R^2 = 0.902$), reflecting enhanced pore diffusion following ibuprofen deprotonation. Similarly, IBU-MIL-100(Fe) was observed to exhibit good fit to IPD model at pH 7.0 and concentration 75 $\mu\text{g mL}^{-1}$ ($R^2 = 0.936$), implying higher intraparticle diffusion at neutral pH value, similar to other findings (W. Sun et al., 2019). Non-zero intercepts ($C = 9.0-201.9 \text{ mg g}^{-1}$) confirmed that film diffusion and pore diffusion occurred simultaneously.

The rate constant (k_{id}) was nearly zero and independent of pH for CIP, indicating fast chemisorption. The change in sign of k_{id} from negative to positive at pH 7.0 is an indication of low competitive desorption due to formation of zwitterion of CIP. The adsorption of PARA was characterized by k_{id} values very close to zero, with weak correlations for IPD ($R^2 < 0.30$), hence intraparticle diffusion is not significant in its adsorption.

3.3.8 Langmuir Dose-Response Analysis in pH systems

The entrapment efficiency (EE%) of ibuprofen, ciprofloxacin, and paracetamol were determined using Cu-BTC and MIL-100(Fe) for MOF concentration between 5 to 75 $\mu\text{g mL}^{-1}$ with pH values of 5 and 7 (Table 1). The Langmuir model was employed for saturated systems, while non-saturated systems were modeled using linear or plateau equations. The ibuprofen showed classic Langmuir behaviour in both MOFs as a result of carboxylate interaction with Cu^{2+} and Fe^{3+} (Figure 9). EE% of Cu-BTC was high (88.1-99.5% at pH 5.0 and 81.7-100% at pH 7.0) while that of MIL-100(Fe) followed Langmuir behavior only at pH 5.0 ($R^2 = 0.745$) while the non-linear behavior at pH 7.0 suggests justifies the contribution from heterogeneous adsorption sites, pore diffusion, or solvent interactions (Figure 9). The EE% of ciprofloxacin remained almost constant at (81-83%) for all concentrations of MOF and at different pH values, revealing that the adsorption of the drug was very effective even at the lowest concentration of drug through a combination of four mechanisms rather than Langmuir monolayer adsorption.

Table 1 Dose-dependent entrapment efficiency (EE%) of ibuprofen, ciprofloxacin, and paracetamol in Cu-BTC and MIL-100(Fe) at pH 5.0 and 7.0 (5-75 $\mu\text{g mL}^{-1}$; drug = 1 mg mL^{-1}), with Langmuir fit parameters for saturation systems and appropriate alternative descriptors for non-Langmuir behaviour.

Drug-MOF Pair	pH	EE 5 $\mu\text{g mL}^{-1}$ (%)	EE 25 $\mu\text{g mL}^{-1}$ (%)	EE 50 $\mu\text{g mL}^{-1}$ (%)	EE 75 $\mu\text{g mL}^{-1}$ (%)	EE_max / Plateau(%)	K_d / Slope	R^2	Dose-Response Pattern
Ibu + Cu-BTC	5.0	88.1	90.4	100	99.5	98.4	$K_d = 0.64 \mu\text{g mL}^{-1}$	0.617	Langmuir ($\uparrow$), saturating
Ibu + Cu-BTC	7.0	81.7	79.8	92.7	100	93.3	$K_d = 0.85 \mu\text{g mL}^{-1}$	0.362	Langmuir ($\uparrow$), saturating
Ibu + MIL-100(Fe)	5.0	84.1	88.9	94.7	98.5	96.0	$K_d = 0.76 \mu\text{g mL}^{-1}$	0.745	Langmuir ($\uparrow$), best overall fit

Ibu + MIL-100(Fe)	7.0	89.9	87.2	97.4	80.7	88.9 (mean EE)	Range = 80.7- 97.4	Mean dev. ± 6.8%	Non-monotonic; 75 µg mL ⁻¹ outlier
Cip + Cu-BTC	5.0	81.9	81.8	83.2	83.5	83.0 (plateau)	Range = 1.7%	Linear R ² = 0.018	Dose- independent; immediate saturation
Cip + Cu-BTC	7.0	83.1	82.6	81.8	80.6	82.1 (plateau)	Range = 2.5%	Linear R ² = 0.974	Dose- independent; slight decrease
Para + Cu-BTC	5.0	91.6	89.3	85.6	82.2	87.2 (mean)	Slope = - 0.136 %/µg	0.998	Anti-Langmuir (↓), linear decrease
Para + Cu-BTC	7.0	92.1	86.1	80.6	79.8	84.7 (mean)	Slope = - 0.178 %/µg	0.899	Anti-Langmuir (↓), linear decrease

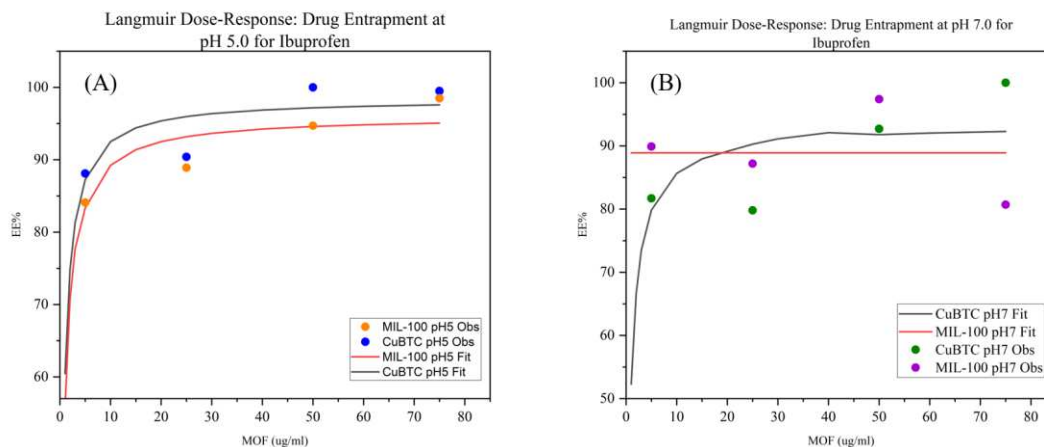


Figure 9. Langmuir adsorption isotherm of ibuprofen on Cu-BTC at (A) pH 5.0 and (B) pH 7.0.

3.4 Cross-Condition Comparative Analysis

3.4.1 Comparative EE% Across Conditions

Cross-condition equilibrium EE% (Table 2) analysis shows consistency in the framework as well as drug-specific absorption trends. IBU follows the hierarchy $ACN \approx pH\ 7.0 > pH\ 5.0$ for

Cu-BTC, which is an influence of ionisation state controlled by pK_a . CIP exhibits dose-independent saturation under all conditions ($EE\% = 81\text{-}100\%$), and the stability in $EE\%$ across varying pH values is a result of the inherent multi-mode binding nature of the fluoroquinolone moiety. PARA exhibits a trend of $ACN \gg pH\ 5.0 \approx pH\ 7.0$, with identical anti-Langmuir trends observed in the two buffer systems and thus, demonstrating pH-independence of H-bond mediated physisorption as the negative control mechanism. The three-drug system in Cu-BTC demonstrates the greatest pH dependency among all cases, $EE\%$ difference of -13.1% between pH 5.0 (87.6%) and pH 7.0 (74.5%) being indicative of increased competition for ionised drugs at neutral pH. On the other hand, pH stability of $EE\%$ for MIX-MIL-100(Fe), $\Delta EE = +2.4\%$, indicates the superior ability to accommodate co-binding due to increased pore size.

Table 2 Comparative $EE\%$ ($t = 24\ h$) across ACN, pH 5.0, and pH 7.0 at highest evaluated dose.

Drug-MOF Pair	$EE\%$ ACN	$EE\%$ pH 5.0	$EE\%$ pH 7.0	Trend	Mechanistic Basis
IBU + Cu-BTC	100.0	99.5	100.0	$ACN \approx pH7 > pH5$	Full $-COO^-$ at pH7 $\rightarrow$ max Cu^{2+} bond
CIP + Cu-BTC	36-100*	83.5	83.1	$pH5 \approx pH7$; ACN dose-dep.	Immediate chemisorption; ACN desorption at high dose
CIP + MIL-100(Fe)	100.0	81.2	78.5	$ACN > pH5 \approx pH7$	Fe^{3+} -fluoroquinolone stable in ACN; buffer reduces net EE via competitive solvation
PARA + Cu-BTC	100.0	82.2-91.6	79.8-92.1	$ACN > pH5 \approx pH7$	H-bond physisorption; pH-insensitive (negative control)
MIX + Cu-BTC	N/A	87.6	74.5	$pH5 > pH7$ ($\Delta EE = -13.1\%$)	Competitive binding amplified at pH7

3.4.2 Integrated Mechanistic Summary

The use of $EE\%$ (entrapment efficiency), k_2 (pseudo-second order rate constants), and k_{id} (intraparticle diffusion constants) was successful in determining the adsorption hierarchy $CIP \geq IBU \gg PARA$, which reflects the effectiveness of the primary adsorption process: bidentate chelation $>$ monodentate carboxyl chelation $>$ hydrogen-bond-mediated physisorption. MIL-100(Fe) was found to be more effective for CIP because of the improved temporal stability and lack of desorption in acetonitrile, while Cu-BTC performed better for ibuprofen adsorption at pH 7.0 because of its unique paddlewheel structure involving Cu^{2+} .

Overall, the kinetics of PSO, nonzero values of Weber-Morris intercept, and Langmuir behaviour suggest a two-step process for adsorption, which includes (i) fast external diffusion of drug molecules to the MOF surface and (ii) slow rate-controlling chemisorption process taking place on the surface of the metal active sites. The intraparticle diffusion takes place secondary and pH-driven for ionizable drugs (IBU, CIP), while for paracetamol hydrogen bonding takes place.

3.5 HPLC-DAD Validation in Real River Water Samples

Matrix-matched calibration curves showed excellent linearity for PARA, CIP, and IBU ($R^2 = 0.9996, 0.9998, \text{ and } 0.9996$, respectively). The analytes exhibited reproducible retention times of approximately 2.85, 4.12, and 7.65 min, respectively, with no interfering peaks detected in the unspiked river-water control. Spike-recovery experiments showed recoveries of 92.8% and 94.1% for PARA, 91.6% and 93.7% for CIP, and 90.9% and 94.5% for IBU at 10 and 100 $\mu\text{g L}^{-1}$, respectively, with RSD values of 1.15-3.45%. These results demonstrate good linearity, accuracy, and precision of the HPLC-DAD method for determination of the three pharmaceuticals in the river-water matrix, supporting its applicability to environmental water analysis and complementing the MOF-based adsorption study (Figure 10).

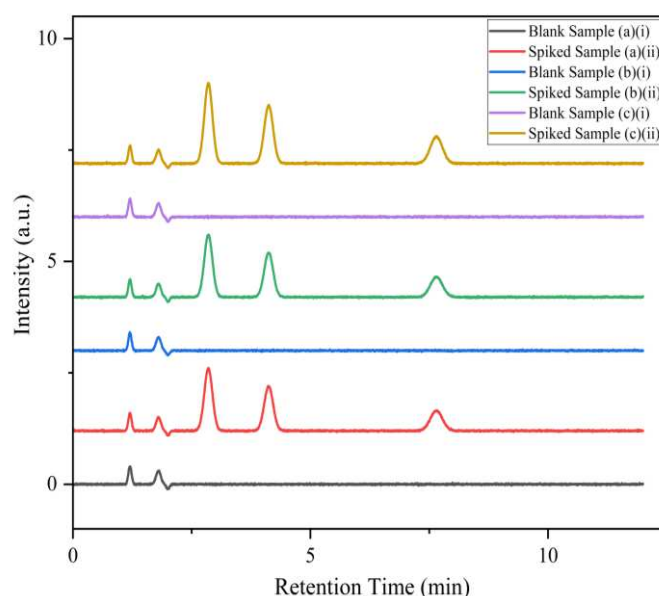


Figure 10 Representative HPLC chromatograms of blank and spiked river-water matrices.

Chromatograms show matrix blanks and samples spiked at 10 and 100 $\mu\text{g L}^{-1}$. Peaks correspond to 1: Paracetamol ($t_R = 2.85$ min), 2: Ciprofloxacin ($t_R = 4.12$ min), and 3: Ibuprofen ($t_R = 7.65$ min). Chromatograms are vertically offset for clarity.

4. Conclusion

This study provides a comprehensive evaluation of the adsorption, encapsulation, and release behaviour of ibuprofen (IBU), ciprofloxacin (CIP), and paracetamol (PARA) using Cu-BTC (HKUST-1) and MIL-100(Fe) under non-aqueous, mildly acidic (pH 5.0), and neutral (pH 7.0) conditions. Chemisorption dominated the adsorption process, with the pseudo-second-order (PSO) model showing excellent correlation ($R^2 = 0.985\text{--}1.000$). Weber–Morris analysis indicated the combined contribution of film and intraparticle diffusion. Adsorption capacity followed the order $\text{CIP} > \text{IBU} > \text{PARA}$, attributed to bidentate chelation, monodentate chelation, and hydrogen-bonding interactions, respectively. IBU exhibited pronounced pH dependence, with PSO rate constants increasing 4.5–9-fold at pH 7.0 due to carboxylate deprotonation. CIP maintained high adsorption across both pH conditions through multiple interaction mechanisms, whereas PARA showed relatively pH-independent adsorption dominated by hydrogen bonding. MIL-100(Fe) demonstrated high stability and CIP loading, while Cu-BTC enabled rapid IBU adsorption at neutral pH. High entrapment efficiencies at low MOF concentrations and predictable pH responsiveness highlight their potential for pharmaceutical remediation and drug delivery. Competitive adsorption in synthetic wastewater confirmed the observed hierarchy, while HPLC-DAD validation in real river water achieved 90–95% recoveries. Overall, these findings support rational MOF selection based on drug chemistry and environmental conditions for pharmaceutical-contaminated water treatment.

5. Declaration of Competing Interests

The authors declare that they have no known competing financial or personal relationships that could have appeared to influence the work reported in this paper.

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7. CRediT Author Contributions

Sujal Balapure: Writing - original draft, Visualization, Writing - review & editing, Formal analysis.

Gitika Kumawat: Writing - original draft, Visualization, Writing - review & editing, Formal analysis, Investigation.

Shivanjali Yadav: Data curation

Pooja Rana: Conceptualization, Supervision, Validation, Writing - review & editing, Project administration.

8. Data Availability Statement

Data sharing is not applicable to this article.

9. Declaration of generative AI and AI-assisted technologies in the manuscript preparation process

During the preparation of this work, the authors used AI-assisted tools for language refinement and structuring. After using these tools, the authors reviewed and edited the content as needed and take full responsibility for the content of the published article.

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