

Supplementary Information

Loading and release of doxorubicin hydrochloride from Iron(III) trimesate MOF and zinc oxide nanoparticle composites

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S 1.1 Synthesis of MIL-100(Fe) Metal Organic Framework

MIL-100(Fe) (henceforth referred as **MF**) was prepared by hydrothermal reaction of trimesic acid (BTC), iron powder, hydrofluoric acid (HF), nitric acid (HNO₃) and water as reported elsewhere^{1,2} with slight modification. Typically, 0.54 g iron powder, 1.35 g of BTC, 0.34 ml of HF, 0.26 ml of HNO₃ and 48 ml of water were mixed through sonication for 1 h. The reaction mixture was then loaded in a teflon lined autoclave and heated at 150 °C for 12 h and subsequently cooled down to room temperature. The light orange MIL-100(Fe) precipitate was further purified to remove impurities. In a typical purification process, about 1 g of MOF was stirred in 500 ml of hot water at 90 °C for 10 h (the water was replaced after 5 h). The MOF was then filtered off when the solution was hot. In the next step, the MOF was stirred in about 100 ml of hot ethanol at 80 °C for about 10 h and filtered off. The solid product thus obtained was finally dried at 150 °C overnight.

MIL-100(Fe) was also prepared without the use of HF (this MOF is henceforth referred as **MNF**). Typically, 8.08 g of Fe (NO₃)₃.9H₂O was completely dissolved in 20 ml of water and then 2.7 g BTC was added to that solution. The mixture was stirred continuously for 1 h at room temperature and then loaded into a teflon lined autoclave. The reaction was allowed to proceed under autogenous pressure for 12 h at 150 °C. The resulting suspension was cooled down to room temperature naturally. The purification step was same as in the case of synthesis for **MF**.³

S 1.2 Material characterization

Powder X-ray diffraction (PXRD) patterns of the samples were obtained at room temperature on a Rigaku (Model: Smart Lab) XRD analyzer operating at 45 kV and 112 mA using Cu K α ($\lambda = 1.5406 \text{ \AA}$) radiation. The Field Emission Transmission Electron Micrographs (FETEM) were recorded using a JEOL (Model: 2100F) instrument with an accelerating voltage of 200 kV. The samples were prepared by drop casting on a carbon coated copper grids of 300 mesh, which were left for overnight for drying. Surface micrographs of synthesized materials were recorded using a Zeiss-Sigma (Model: Sigma 300) Field Emission Scanning Electron Microscope (FESEM) at an accelerating voltage of 2-5 kV. The samples were placed on an aluminium stub containing carbon tape and coated with conducting layer of gold using a sputtering unit for 120 seconds before the analysis. The mapping was done using energy dispersive X-ray spectroscopy (EDX) by Oxford Instruments UK at an accelerating voltage of 20 kV using Aztec software. Nitrogen adsorption/ desorption isotherm was recorded on Quantachrome automated volumetric gas sorption analyzer (Autosorb iQ) at -196 °C. The samples were degassed at 150 °C for 12 h in ultrahigh vacuum. Specific surface area (S_{BET}) was calculated by Brunauer–Emmett–Teller (BET) method between the relative pressure (p/p_0) of 0.05 to 0.25. The pore volume (v_p) was calculated by volume adsorbed basis at a relative pressure of 0.99. The thermal stability of the samples was characterized using Netzsch Thermo Gravimetric Analyzer (TGA). About 10 mg of the sample was heated at a rate 10 °C min⁻¹ between 30–800 °C under nitrogen flow. The drug concentration in the liquid solution was determined by measuring the absorbance at a wavelength of 480 nm using UV-Visible spectrophotometer (Model Orion AquaMate 8000, Thermo Scientific).

S 1.3 DOX Loading in MOF composites

The DOX loading experiments were performed using the protocol from the literature.¹ At first, the carrier sample was dried at 100 °C for about 4 h to remove the moisture. About 100 mg of this dried carrier was added to 15 ml of 2 mg/ml DOX solution and kept under dark in an orbital shaker at 200 rpm and 25 °C for about 24 h. The sample was recovered in a high speed centrifuge (run at 10,000 rpm for about 10 mins). The concentration of DOX in the supernatant was measured via its absorbance using a UV-Visible spectrophotometer at 480 nm.

S 1.4 Description of release medium

The DOX release experiments were carried out in the phosphate buffer saline (PBS) solution of pH 7.4. Typically, for making of 1 L PBS, following reagents NaCl (8.0 g), KCl (0.2 g), Na₂HPO₄ (1.42 g) and KH₂PO₄ (0.24 g) were dissolved in 800 ml of water. The pH of the solution was about 7.4. Finally, necessary amount of additional water was added to makeup the solution to 1L.⁴

S 1.5 Release of DOX from MOF composites

The DOX release experiments were carried out by the protocol similar to as described in literature.^{1, 5} The drug release behaviour of the DOX-carriers was studied by dispersing the composites in ~15 ml of phosphate buffer saline (PBS) of pH 7.4 at 37 °C. All the experiments were carried out in an orbital shaker with shaking motion of 200 rpm. The release profile was obtained by measuring the supernatant concentration in the PBS at periodic intervals. At each sampling time, the composites were completely separated from the PBS in a centrifuge at 10,000 rpm for 10 min. An equal volume of fresh PBS was added after each sampling and the release experiment was continued. The DOX concentration in the sampled supernatant PBS was analyzed using a UV-Visible spectrophotometer.

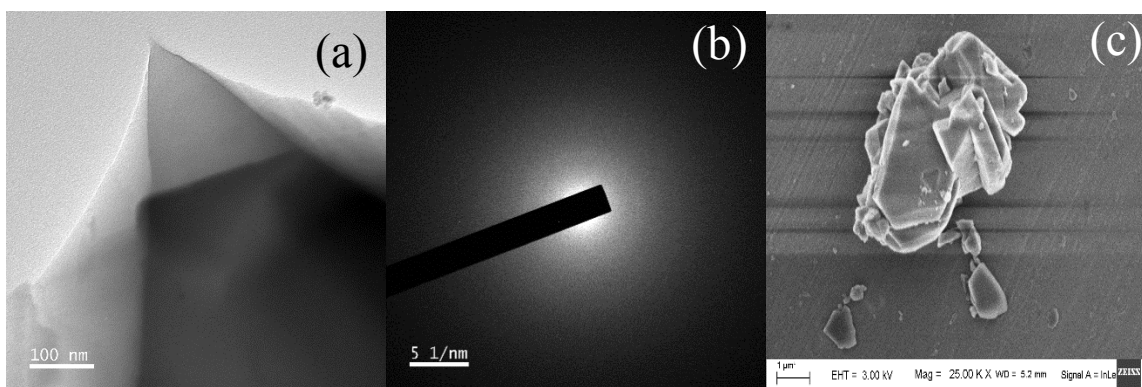


Fig. S1. (a) FETEM image, (b) SAED pattern of **MF** and (c) SEM image of DOX loaded **MF**

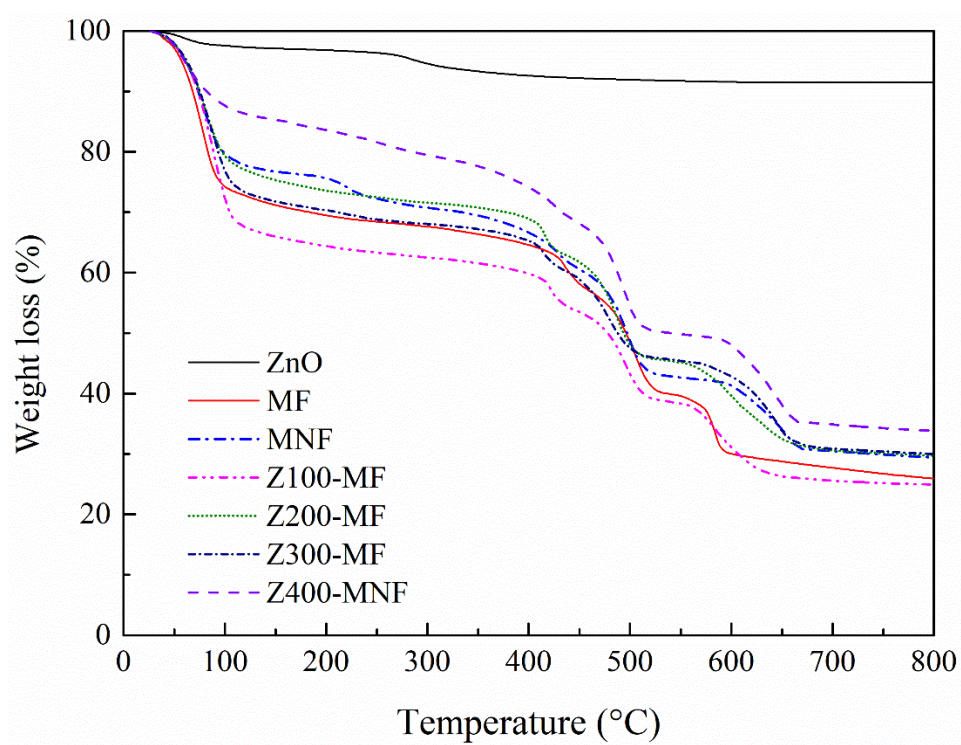


Fig. S2. TGA curves of ZnO, **MF**, **MNF**, **Zw-MF** and **Zw-MNF** composites

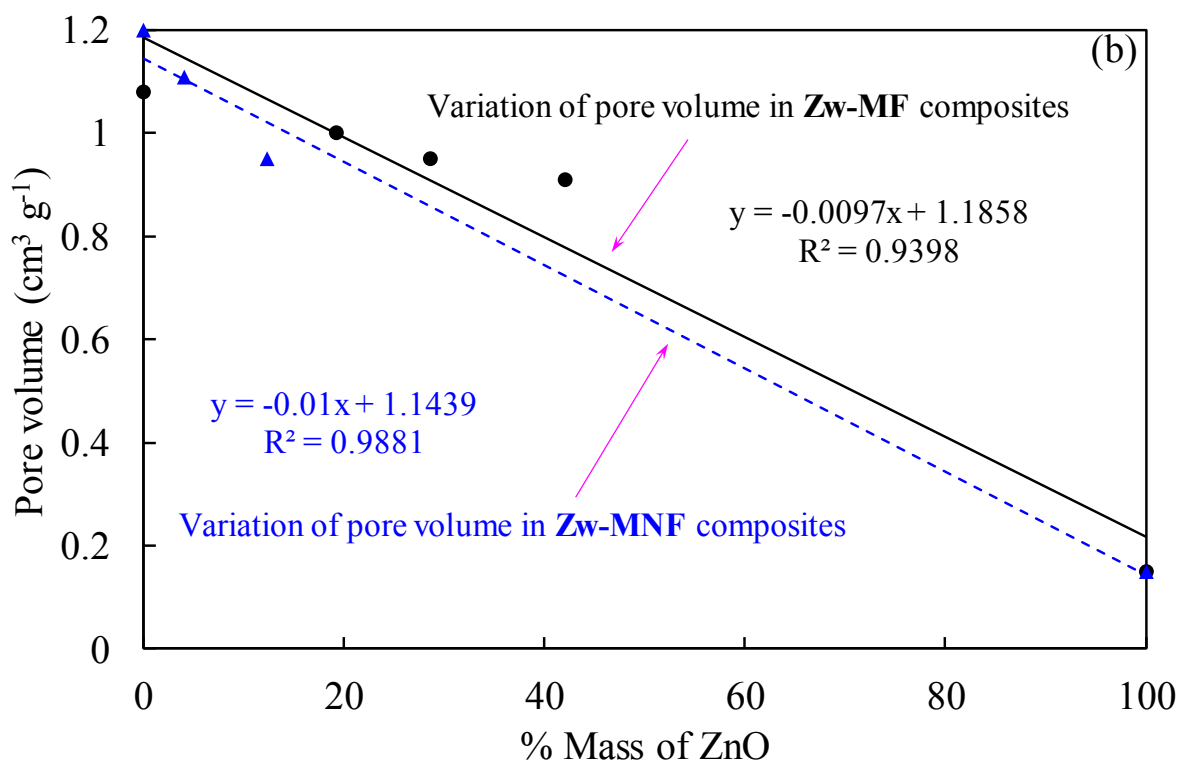
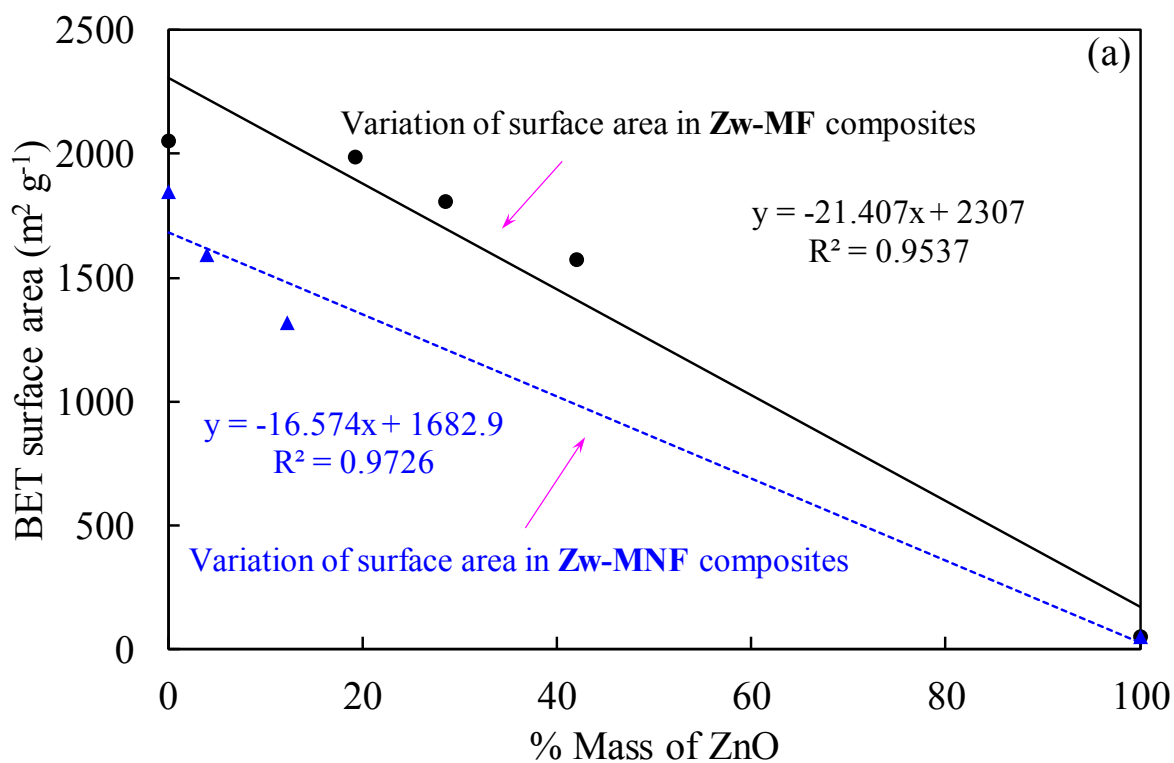


Fig. S3. Variation of (a) surface area and (b) pore volume with mass percentage of ZnO in **Zw-MF** and **Zw-MNF** composites

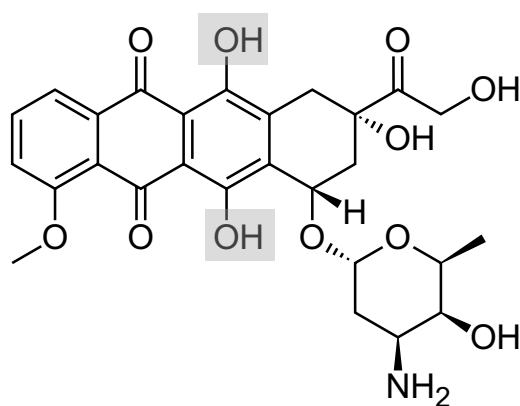


Fig.S4: Structure of DOX highlighting hydroxyl groups of the aglycone moiety. They act as potential binding sites with the metal centers in MIL-100(Fe).

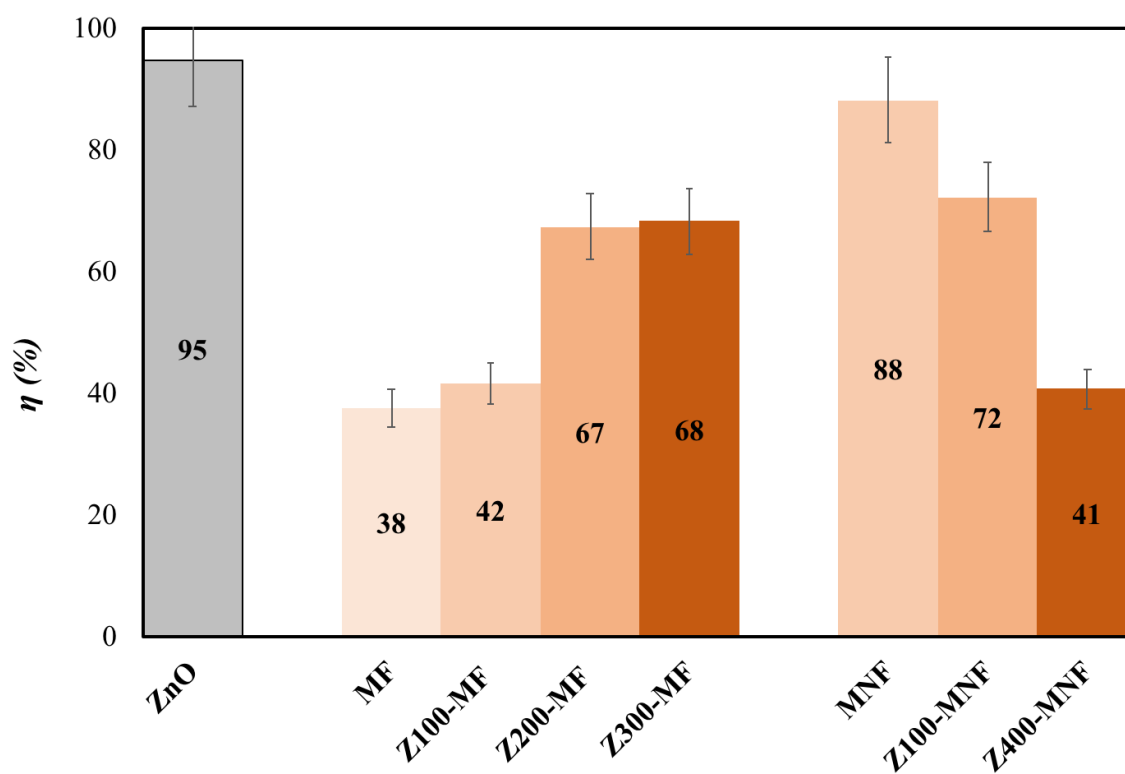


Fig. S5. DOX entrapment efficiencies of ZnO, Zw-MF and Zw-MNF composites

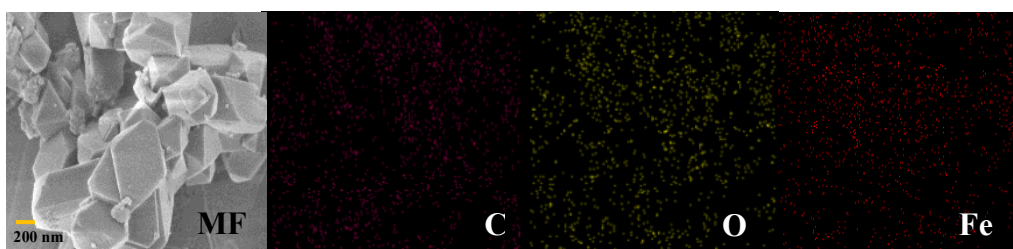


Fig. S6. EDX mapping of pure MIL-100(Fe)

Table S1: DOX loading capacity of $\text{Fe}_3\text{O}_4@MF$ and $\text{Fe}_3\text{O}_4@MNF$ composites

Sr. No.	Composites	Fe_3O_4 nanoparticle (wt %)	q (mg of DOX/g of carrier)
1	Fe_3O_4	Pure	110
2	MF	-----	107
3	F125-MF	16	194
4	MNF	-----	234
5	F027-MNF	1.0	267
6	F200-MNF	6.7	150
7	F1000-MNF	31.5	84

References

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