Electronic Supplementary Material (ESI) for Journal of Materials Chemistry B

Impact of phosphorylation over the encapsulation of nucleosides analogues within porous iron(III) Metal Organic Frameworks MIL-100(Fe) nanoparticles.

Supplementary Information

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1. Kinetics of encapsulation of different AZT derivatives at different payloads

Tab. S1: *Kinetics of Encapsulation of different AZT-TP payloads within MIL-100 nanoMOFs defined as encapsulation efficiency (EE, %) and drug payload (Payload, wt%).*

	TL =8 wt%		TL =19 wt%		TL =25.4 wt%	
Incubation Time (h)	**EE (%)[a]**	**Payload (wt %)[b]**	**EE (%)[a]**	**Payload (wt %)[b]**	**EE (%)[a]**	**Payload (wt %)[b]**
0.5	100	8	98.9 ±0.3	18.9 ±0.1	77.8 ±3.2	19.7 ±0.8
4	100	8	99.4 ±0.4	18.9 ±0.1	85.3 ±4.8	21.6 ±1.2
8	100	8	97.1 ±2.9	18.5 ±0.5	89.1 ±2.8	22.6 ±0.7
24	100	8	99.5 ±0.5	19 ± 0.1	93.4 ±2.4	23.7 ±0.6

Tab. S2: *Kinetics of Encapsulation and AZT-MP payloads within MIL-100 nanoMOFs defined as encapsulation efficiency (EE, %) and drug payload (Payload, wt%).*

	TL =8 wt%		TL =19 wt%		TL =25.4 wt%		TL =40 wt%	
Incubation Time (h)	**EE (%)[a]**	**Payload (wt %)[b]**	**EE (%)[a]**	**Payload (wt %)[b]**	**EE (%)[a]**	**Payload (wt %)[b]**	**EE (%)[a]**	**Payload (wt %)[b]**
0.5	100	8	99.5 ±0.5	19 ±0.1	100 ±0.1	25.4 ±002	87.8 ±1.7	35.1 ±0.7
4	100	8	99.4 ±0.7	19 ±0.1	99.9 ±0.1	25.4 ±0.1	94 ±8	37.6±3.2
8	100	8	99.2 ±0.5	18.9 ±0.1	99.8 ±0.1	25.3 ±0.1	88.3 ±0.1	35.3±0.1
24	100	8	99.5 ±0.7	19 ± 0.1	100 ±0.1	25.4 ±0.01	94.3 ±7.5	37.3 ±3

Tab. S3: *Kinetics of Encapsulation and AZT payloads within MIL-100 nanoMOFs defined as encapsulation efficiency (EE, %) and drug payload (Payload, wt%).*

	TL =13.4 wt%	
Incubation Time (h)	**EE (%)[a]**	**Payload (wt %)[b]**
0.5	8.7 ±6.2	1.2 ±0.8
4	8.5 ±3	1.1 ±0.4
8	9.1 ±2.1	9.1 ±2.1
24	9.1 ±3.7	1.2 ± 0.5

[a] encapsulation efficiency = $EE\,(\%) = \frac{encapsulated\ Drug\,(mg)}{Drug\ Solution\,(mg)} \times 100$

[b] payload = $Payload\,(wt\%) = \frac{encapsulated\ Drug\,(mg)}{MIL-100\ nanoMOFs\,(mg)} \times 100$

2. NanoMOFs interaction with aqueous solutions of a phosphate salt evaluated by ITC

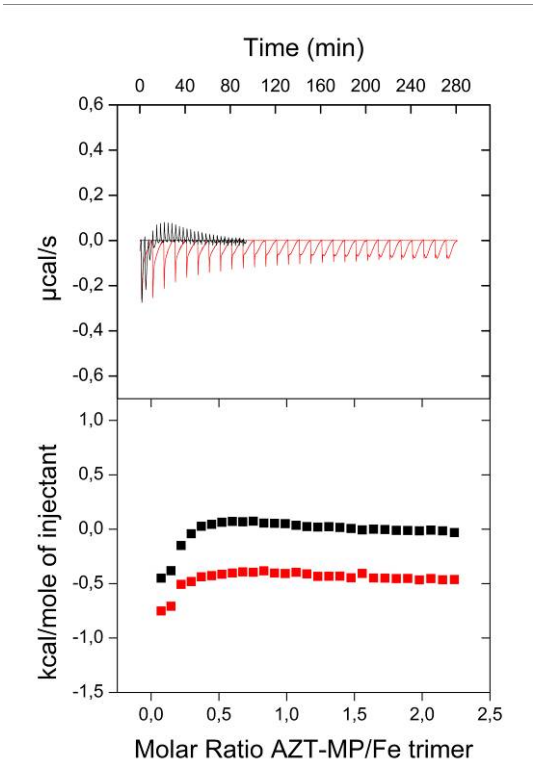


Fig. S1: *AZT-MP (5 mM) dilution in water (red) or titration into a nanoMOFs aqueous solution 0.5 mM (black).*

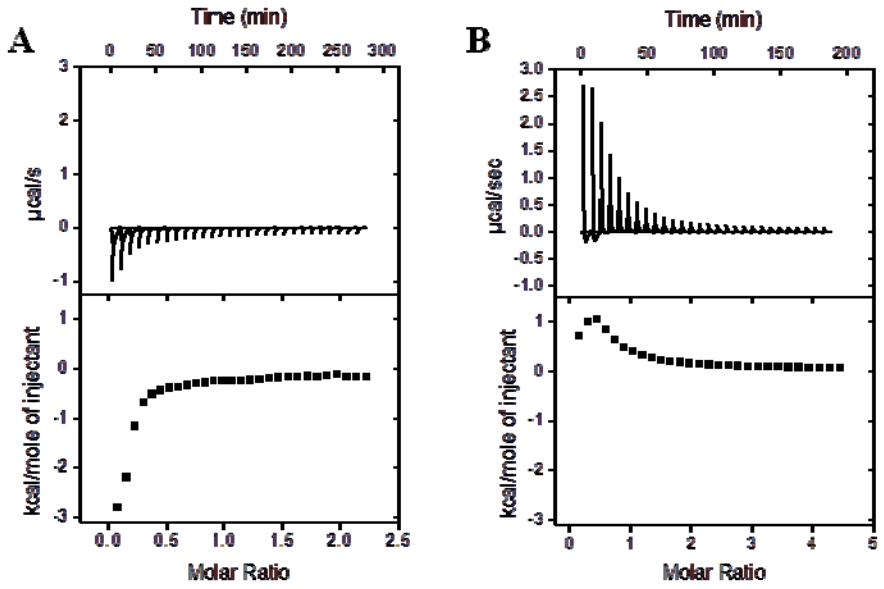


Fig. S2:*MIL-100 nanoMOF (0.5 mM) binding isotherms of a K_2HPO_4 aqueous solution 5 mM (A) or 10 mM (B).*

3. UV-visible absorption and circular dichroism titration of AZT-TP with nanoMOFs in PBS

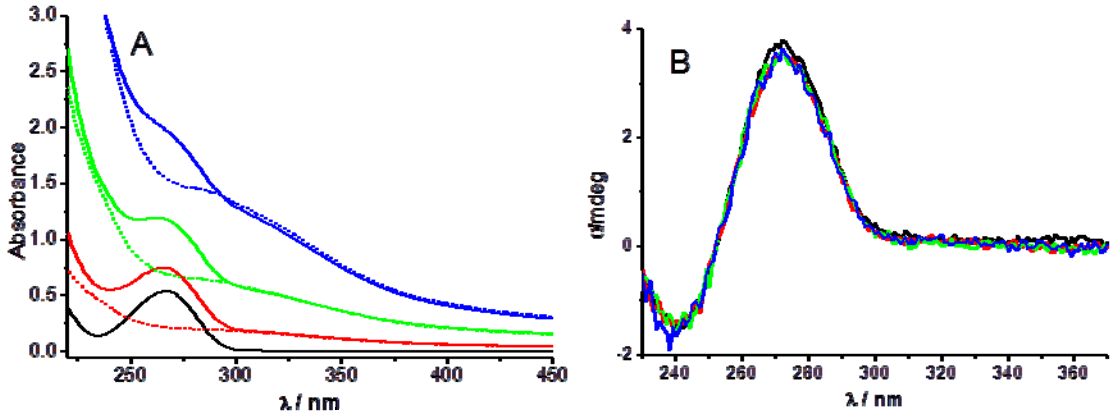


Fig. S3: *UV-visible absorption (A) and circular dichroism (B) titration of AZT-TP with MOF in PBS buffer (10-^{2} M, pH 6.5) at 22°C, cell pathlength 0.5cm, T=22 °C. Color code: drug alone, black solid; drug mixed with MOF , colored solid: 0.0 3 (red), 0.1 (green), 0.2mg/ml (blue). MOF alone (same color code, dotted lines).*

4. UV-visible absorption and circular dichroism titration of AZT-TP with nanoMOFs in PBS

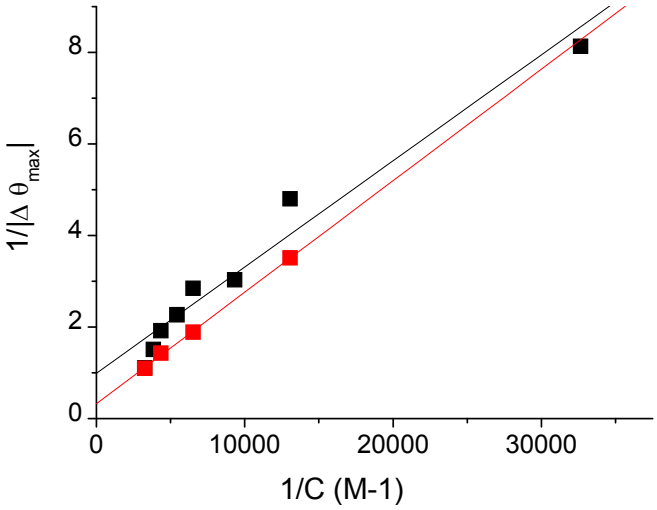
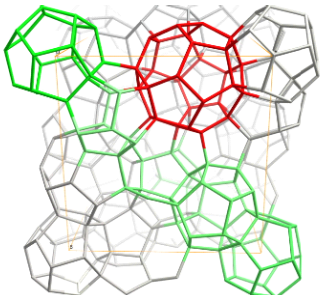


Fig.S4*: Plot of reciprocal $\Delta\theta$ at λ_{max} vs. reciprocal iron(III) trimer concentration after 24 h from preparation of the mixtures of AZT-TP (black) or AZT-MP (red) 1×10^{-4} M and MIL-100 nanoMOFs from 0.02 to 0.20 mg/mL, in water, cell path 0.2 cm, T = 22°C.*

Available Iron sites occupancy

Zeotype architecture MTN = $2[5^{12}] + [5^{12}.6^4]$



$[5^{12}]$ = small mesoporous cages (SC) delimited by 12 microporous pentagonal windows

$[5^{12}.6^4]$ = large mesoporous cages (LC) delimited by 12 microporous pentagonal windows and 4 microporous hexagonal windows

20: Iron trimers/SC

28: Iron trimers/LC

$$Iron\ trimers_{LC}\ \% = \frac{Iron\ trimers_{LC}}{Iron\ trimers_{MIL100}}\ \% = \frac{28}{2[20] + 28}\ \% = 41.18\ \%$$

i) Iron sites occupancy by AZT-TP

Maximum experimental AZT-TP payload = 24.4 wt %

Molar weight (Mw) MIL-100 per iron trimer = 653 g mol^{-1}

Mw AZT-TP = 507,2 g mol^{-1}

The number of mol of AZT-TP per mol of trimer is deduced from :

$$\frac{AZTP_{mol}}{MIL100\ trimers_{mol}} ratio = 0.314$$

This gives 31.4 AZT-TP molecules/100 trimers $_{MIL100}$

Considering that only the large cages are accessible to the drug, there are:

31.4 AZT-TP/41.18 trimers $_{LC}$ = **0.76** AZT-TP molecules/ trimers $_{BC}$

This means that there is roughly one AZT-TP molecule interacting with each iron trimers within the large cages.

As each BC contains 28 trimers, there are about **21** AZT-TP molecules/LC

ii) Iron sites occupancy by AZT-MP

Maximum experimental AZT-MP payload = 36 wt %

Molar weight (Mw) MIL-100 per iron trimer = 653 g mol^{-1}

Mw AZT-TP = 381.28 g mol^{-1}

The number of mol of AZT-TP per mol of trimer is deduced from:

$$\frac{AZTMP_{mol}}{MIL100\ trimers_{mol}} ratio = 0.617$$

This gives 61.7 AZT-TP molecules/100 trimers $_{MIL100}$

Considering that only the large cages are accessible to the drug, there are:

61.7 AZT-TP/41.18 trimers $_{LC}$ = **1.5** AZT-TP molecules/ trimers $_{BC}$

Considering that two over three iron metal sites are accessible per trimer (the third site being occupied by oxide group) this means that there is roughly 1.5 AZT-TP molecule interacting with both the available metallic site per each iron trimer within the large cages.
As each BC contains 28 trimers, there are about **42** AZT-MP molecules/LC