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Design of Zr-based metal organic framework as an efficient fosfomycin carrier: a combined experimental and DFT study

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Supporting Information

Loading Efficiency;

The loading efficiency was calculated by using LC-MS/MS analysis. Analysis was performed at METU Central Laboratory, Molecular Biology-Biotechnology Research and Development Center, Mass Spectroscopy Laboratory, Ankara, Turkey. The mother liquor or supernatant of UiO-66/FOS synthesis was analyzed by liquid chromatography-mass spectrometry (LC-MS/MS, AGILENT 6460 Triple Quadropule System coupled with AGILENT 1200 series HPLC) to determine the fosfomycin loading efficiency into UiO-66 nanocrystals. Free fosfomycin amount in the mother liquor was used to calculate the LE by the following equation:

$$\text{LE (\%)} = \frac{total\ amount\ of\ FOS\ in\ the\ reaction\ medium - FOS\ amount\ in\ the\ mother\ liquor}{total\ amount\ of\ FOS\ in\ the\ reaction\ medium}$$

Loading efficiencies were calculated as %87.7±6.4, %90.8±3.0, %89.7±4.1 and %70 for UiO-66/FOS-1, UiO-66/FOS-2, UiO-66/FOS-3 and UiO-66/FOS-AD, respectively.

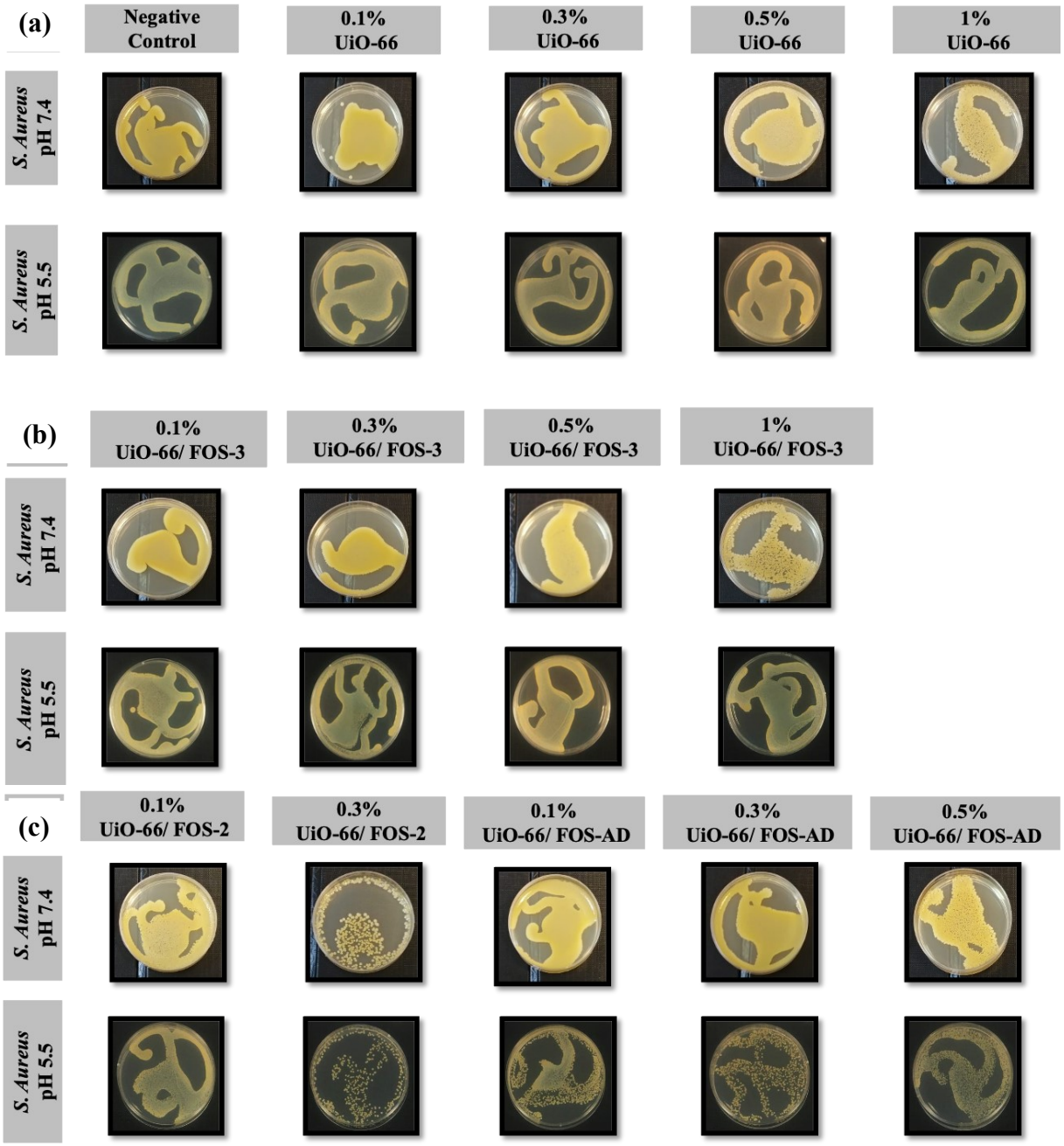

Fig. S1. Images of colonies on MH agar at the end of 18-24 hours of incubation at either pH 5.4 or 7.4 and microorganism was used as the negative control. (a) UiO-66 nanocrystals without FOS loading for all concentrations, (b) UiO-66/FOS-3 applied at 0.1%, 0.3%, 0.5% and 1% (w/v) (c) UiO-66/FOS-2 and UiO-66/FOS-AD applied at 0.1% and 0.3% (w/v).

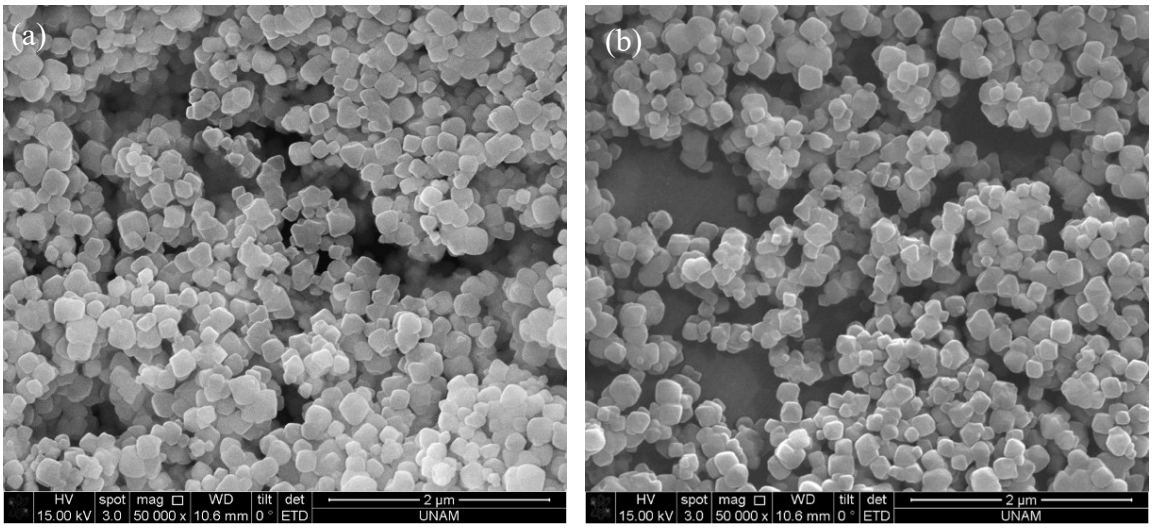

Fig S2. SEM images of UiO-66 nanocrystals after 24 h aging in PBS at (a) pH 7.4, (b) pH 5.5

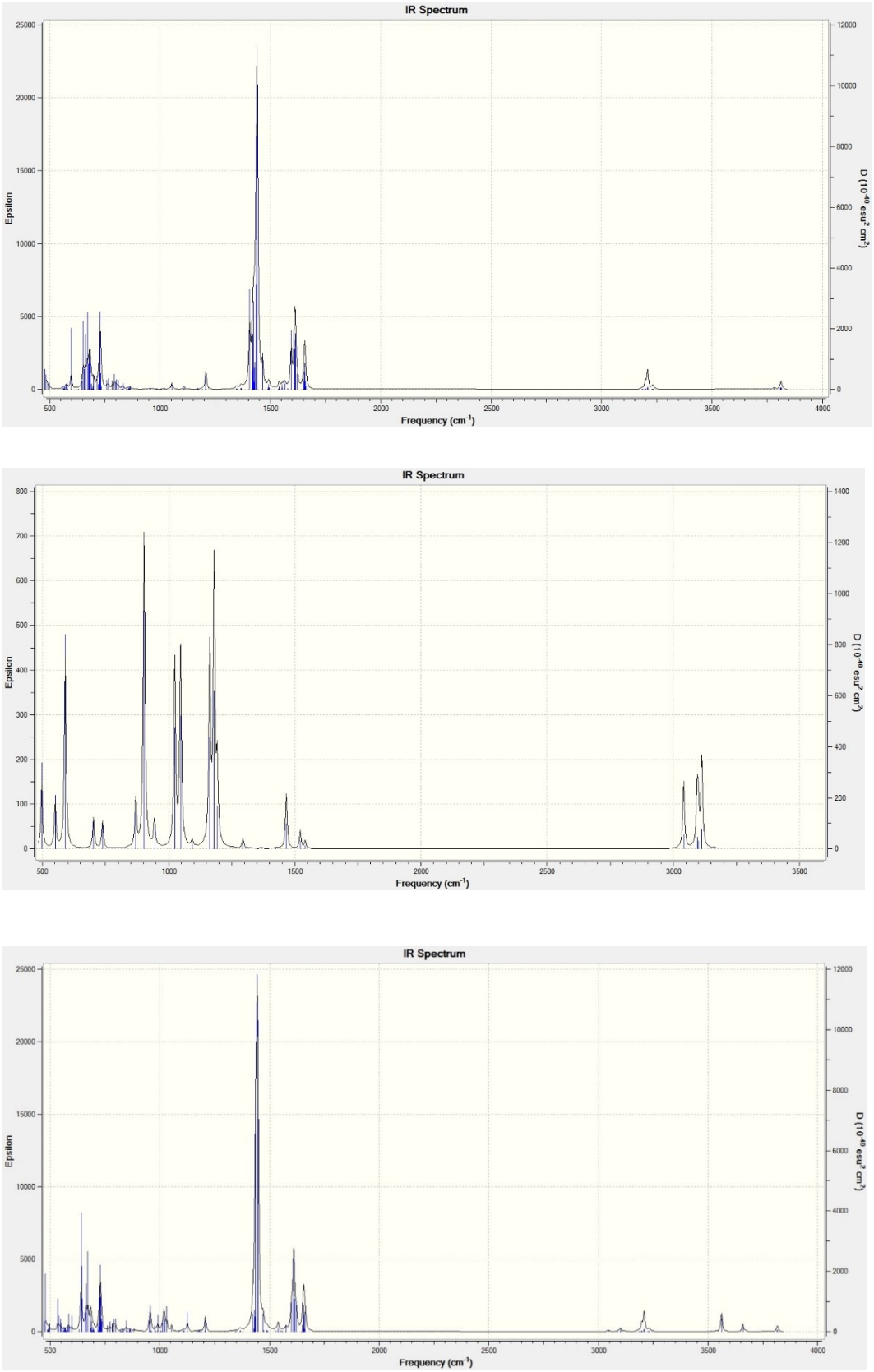

Fig. S3. Theoretical IR spectra of defective UiO-66 (top), Fosfomycin (middle), and UiO-66/FOS-AD (bottom) obtained from the B3LYP/6-31G(d) calculations.

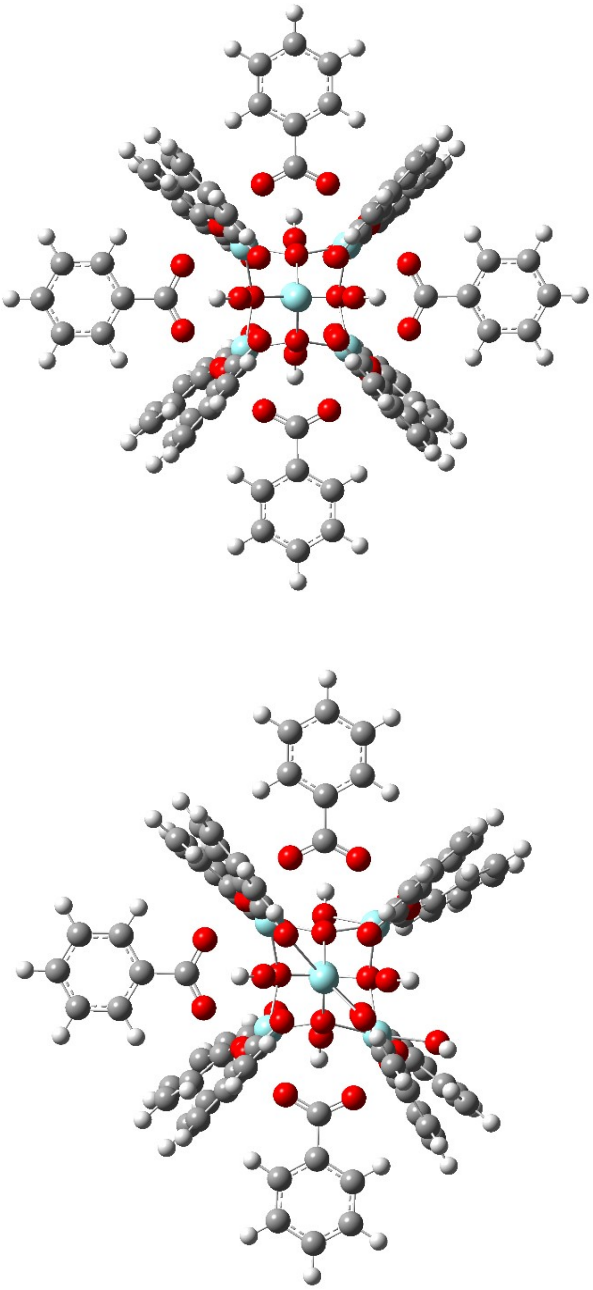

Fig. S4. Pristine (top) and defective (bottom) UiO-66 clusters optimized at the B3LYP/6-31G(d) level of theory.

The minimum bactericidal concentration (MBC);

The antibiotic concentrations used for loading to UiO-66 nanocrystals were selected based on the minimum free fosfomycin concentration that had a cidal effect (MBC) on the growth of *Staphylococcus aureus* ATCC 6538 and *Escherichia coli* ATCC 25922 strains. To determine the minimum bactericidal concentration values, pathogen test microorganisms were cultured at eleven different free antibiotic concentrations. The MBC value was recorded as 0.128 mg/mL for both strains. To retain the antibiotic-induced antimicrobial activity in UiO-66/FOS nanocrystals, two different concentrations of 0.8333 and 0.416 mg/mL, which are higher than the MBC value, were selected for Fosfomycin loading. These concentrations were selected by considering two factors i.e., i) the loading efficiency of the fosfomycin antibiotic to the UiO-66 nanocrystals, and ii) the release behavior of the antibiotic from the UiO-66 nanocrystals.

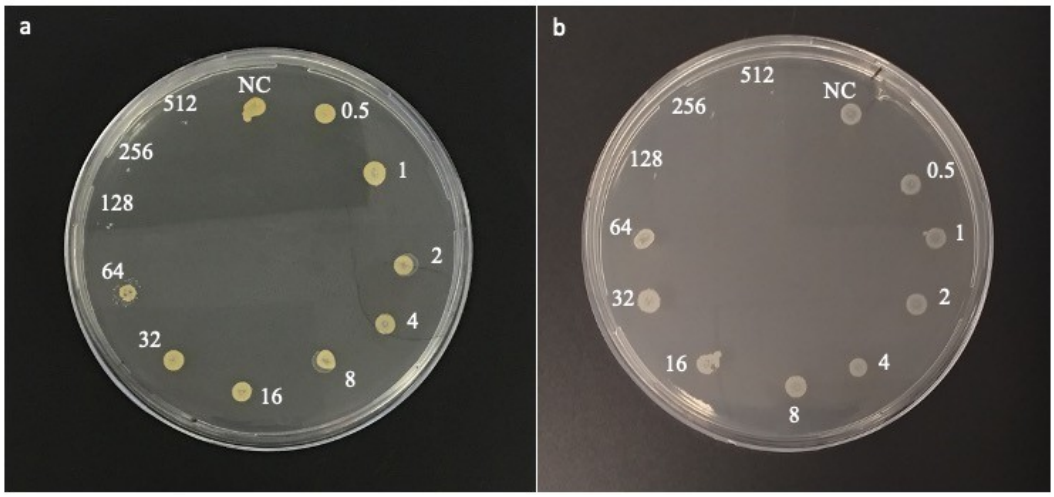

Fig. S5. The minimum bactericidal concentration (MBC) values of free fosfomycin antibiotic (µg/mL); (a) *Staphylococcus aureus* ATCC 6538, (b) *Escherichia coli* ATCC 25922. NC: Negative control.