Supplementary Information

Hollow Microporous Organic Capsules

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Experiment

Materials. Anhydrous ferric chloride ($FeCl_3$), tetraethyl orthosilicate (TEOS), ammonia water ($NH_3 \cdot H_2O$), 1,2-dichloroethane (DCE), styrene (St), hexane, $NaHCO_3$, sodium dodecyl benzene sulfonate (SDBS), methanol and absolute ethanol were analysis grade and purchased from National Medicines Corporation Ltd. of China. Divinylbenzene (DVB, Aldrich, 80 % grade), and formaldehyde dimethyl acetal (FDA, Aladdin, 98 %) were used as received. Potassium persulfate ($K_2S_2O_8$, Fisher) was recrystallized from deionized water prior to drying under reduced pressure. 3-(trimethoxysilyl)propyl methacrylate (MPS) and other reagents of analytical grade were utilized without further purification.

Preparation and surface modification of silica nanoparticles. The 130nm silica nanoparticles were synthesized in ethanol according to the Stöber method. Ethanol (500 ml) and TEOS (40 ml) were mixed by vigorously mechanical agitation in a 1000 ml three-necked round bottom flask and followed by adding $NH_3 \cdot H_2O$ (40 ml). After stirring 24 h, a mixture of MPS and ethanol (4 ml: 26 ml) was dropped into the dispersion of SiO_2 spheres in ethanol. 24 h later, After three cycles of centrifugation and redispersion with ethanol, then dried in vacuum oven, the surface modification of silica nanoparticles (SiO_2-MPS) were obtained. The 200 nm silica nanoparticles were synthesized by using similar methods, only change the amount of $NH_3 \cdot H_2O$ to 50 ml.

Preparation of SiO_2@PS-DVB nanoparticles. The SiO_2@PS-DVB nanoparticles were obtained by emulsion polymerization. In a typical experiment, SDBS (0.032 g) as emulsifier and $NaHCO_3$ (0.24 g) as buffer agent dissolved in distilled water (100 ml) was added in a 500 ml three-necked round bottom flask, then adding the dispersion of SiO_2-MPS (1.2 g, 130 nm) in ethanol (10 ml).After adding the styrene (2.5ml, 5ml, 10 ml, 15ml) and DVB as comonomer and $K_2S_2O_8$ as initiator. The emulsion polymerization was heated at 85 ºC under inert gas protection for 90 min.

The emulsion of SiO_2@PS-DVB was centrifuged (8000 rpm) for 10 min and then dried in vacuum oven to get SiO_2@PS-DVB nanoparticles.

Preparation of hollow microporous organic capsules (HMOCs). The SiO_2@PS-DVB (1.0 g) was swollen in DCE (20 ml) about 1 h. FDA (1.73 ml) was added to the mixture and then added $FeCl_3$ (3.11 g). The Friedel-Crafts-type hypercrosslinking reaction was stirred at 45 ºC for 5 h to form original network, then heated at 80 ºC for 19 h. The resulting microporous nanoparticles were filtered and washed three times with methanol followed washed with methanol in a Soxhlet for 24 h, and used HF to etch the silica core, finally dried in vacuum oven at 60 °C for 24 h. The brown HMOCs were obtained.

Drug loading and release. The loading of the drug was carried out by the immersion of HMOCs in ibuprofen hexane solution with a certain concentration. A typical procedure for loading ibuprofen in HMOCs was as follows: 150 mg of HMOCs was suspended in 5 ml of 90 mg/ml ibuprofen hexane solution under stirring for 96 h while preventing the evaporation of hexane. The drug-loaded sample was separated from the solution by vacuum filtration, washed with hexane, and dried at room temperature. Filtrate was sucked and properly diluted to determine the drug-loading amount by UV-Vis spectrophotometer.

After the drug-loaded samples (200 mg) transferring to semipermeable bag, the release rate was obtained by soaking the drug-loaded samples in 100 ml of simulated body fluid (PBS, pH = 7.4, buffer solution, 37 ℃) at predetermined time intervals, 3 ml samples were withdrawn and replenish 3 ml PBS immediately. Samples were analyzed for ibuprofen content at 263 nm using UV-Vis spectrophometer.

Viability of cells in the presence of HMOCs using MTT assay

The viability of cells in the presence of 10 % - HMOCs was investigated using 3-[4,5-dimethylthialzol-2-yl]-2,5-diphenyltetrazolium bromide (MTT, Sigma) assay. For MTT assay, HepG2 cells were seeded into 96-well plates at a density of 1×10^4 per well in 100 μL of media and grown. The cells were then incubated with various concentrations of HMOCs for 48 h. Following this incubation, cells were incubated in media containing 0.5 mg ml^{-1} of MTT for 4 h. The precipitated formazan violet crystals were dissolved in 100 μL of 10 % SDS in 10 mmol HCl solution at 37 °C overnight. Data are presented as mean ± SEM, n = 4-5. Statistical significance was determined by ANOVA followed by the Dunnett's Multiple Comparison Test. No significant difference was found.

Utilization of HMOCs as Confined Microreactors

The HMOCs were dispersed in 0.4 M $FeCl_3$ and 0.2 M $FeCl_2$ aqueous solution. These HMOCs were separated by centrifugation, washed by methanol and redispersed in toluene and then mixed with ammonia water, which can obtain nanoscale magnetic particles inside the hollow.

Characterizations.

Polymer surface areas, N_2 adsorption isotherms (77.3 K) and pore size distributions were measured using Micromeritics ASAP 2020 M surface area and porosity analyzer. Before analysis, the samples were degassed at 110 °C for 8 h under vacuum (10^{-5} bar). Transmission electron microscopy (TEM) images were taken on a Tecnai G20 microscope (FEI Corp. USA) instrument operated at an accelerating voltage of 200 kV. Particle Sizer with DLS (Dynamic Light Scattering) and NIBSTM (Non-invasive Back Scatter) technology from Malvern Instruments (Malvern, UK) and the effective detection capability is 0.6-6000 nm. Thermogravimetric (TG) analyses were

carried out between room temperature and 900ºC under nitrogen atmosphere, using a Perkin Elmer Diamond TG/DTA. The heating rate was 10 ºC·min^{-1}. Magnetic properties were recorded on a Magnetic Property Measurement System MPMS XL-7 (Quantum Design, UK) at 300 K.

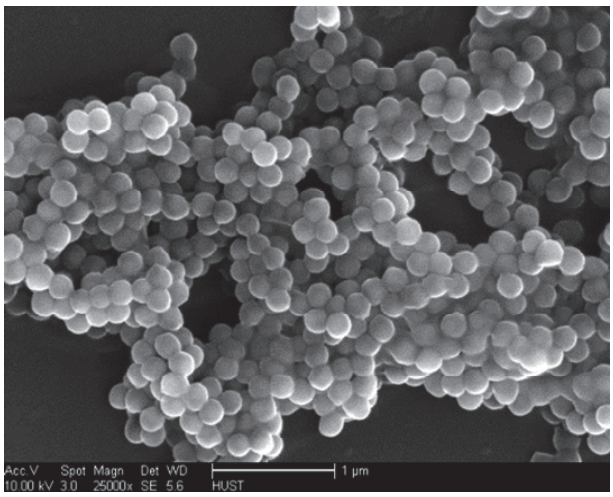


Figure S1. SEM image of SiO_2@PS-0.5 % DVB. The SiO_2 nanoparticles core is 130 nm. The scale is 1 µm.

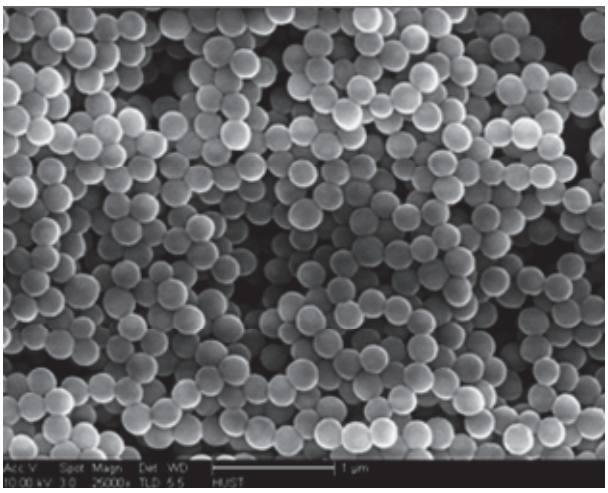


Figure S2. SEM image of SiO_2@PS-1 % DVB. The SiO_2 nanoparticles core is 130 nm. The scale is 1 µm.

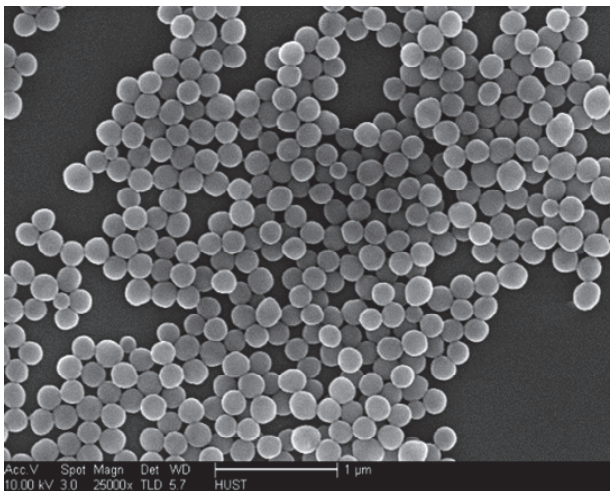


Figure S3. SEM image of SiO_2@PS-2.5 % DVB. The SiO_2 nanoparticles core is 130 nm. The

scale is 1 μm.

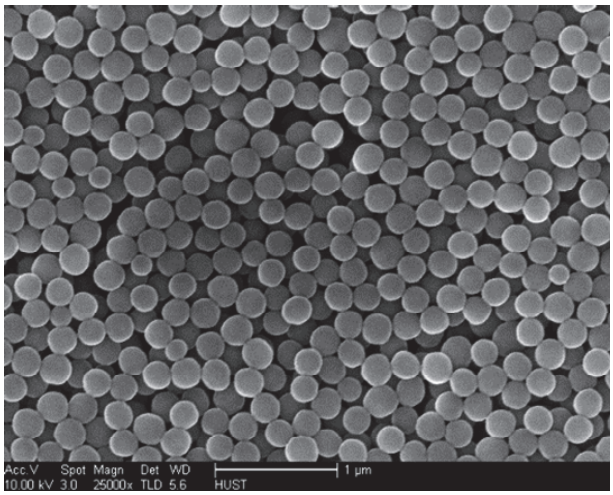


Figure S4. SEM image of SiO_2@PS-5 % DVB. The SiO_2 nanoparticles core is 130 nm. The scale is 1 μm.

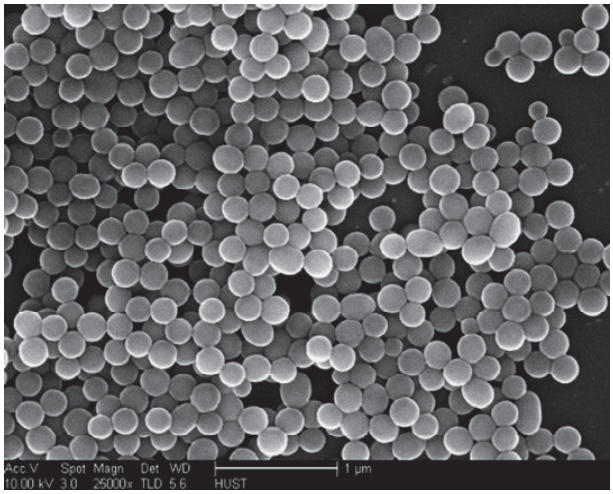


Figure S5. SEM image of SiO_2@PS-10 % DVB. The SiO_2 nanoparticles core is 130 nm. The scale is 1 μm.

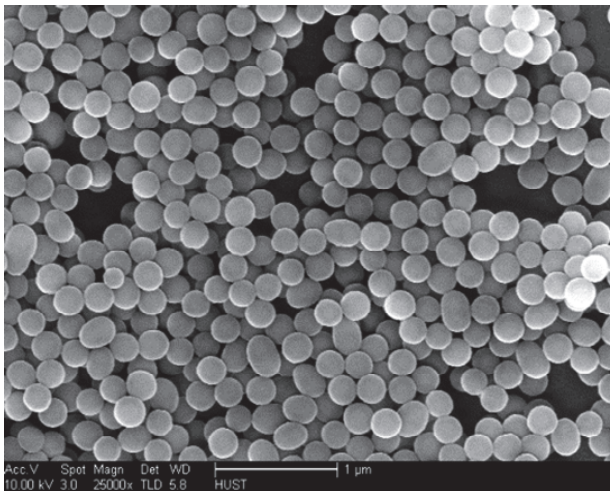


Figure S6. SEM image of SiO_2@PS-15 % DVB. The hollow cavity is 130 nm. The scale is 1 μm.

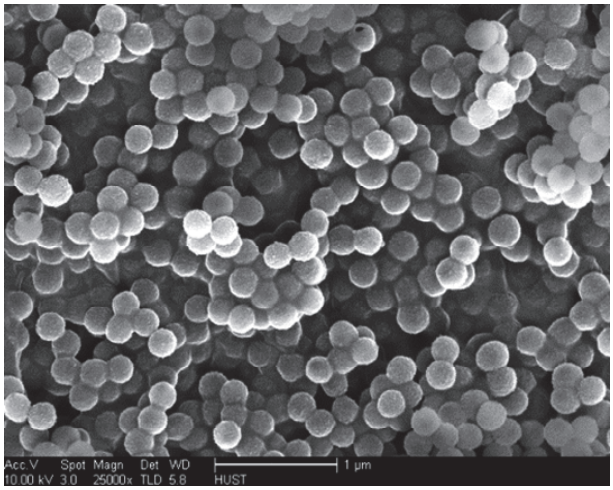


Figure S7. SEM image of 0.5 % - HMOCs. The hollow cavity is 130 nm. The scale is 1 µm.

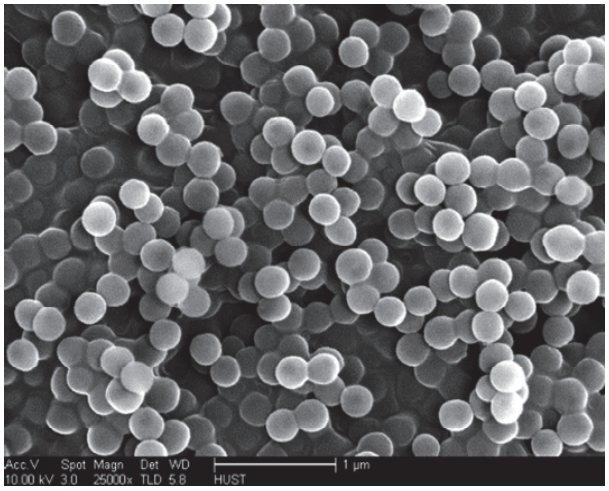


Figure S8. SEM image of 1 % - HMOCs. The hollow cavity is 130 nm. The scale is 1 µm.

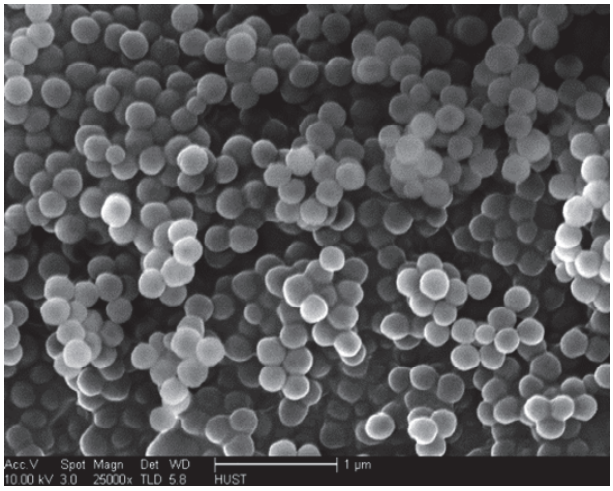


Figure S9. SEM image of 2.5 % - HMOCs. The hollow cavity is 130 nm. The scale is 1 µm.

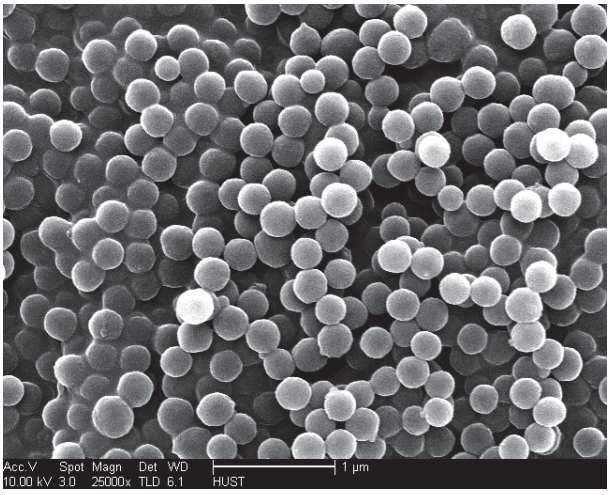


Figure S10. SEM image of 5 % - HMOCs. The hollow cavity is 130 nm. The scale is 1 µm.

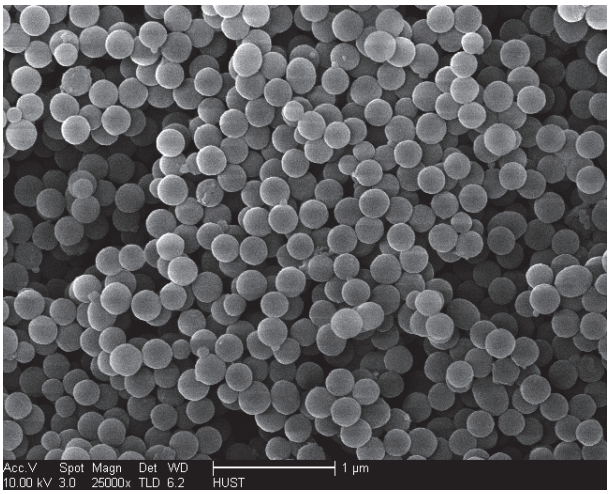


Figure S11. SEM image of 10 % - HMOCs. The hollow cavity is 130 nm. The scale is 1 µm.

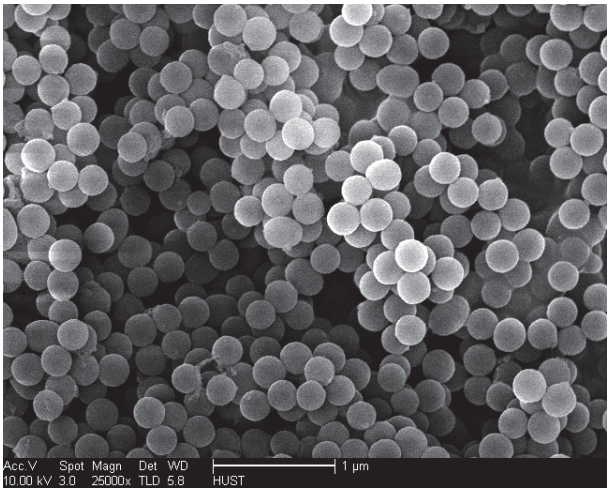
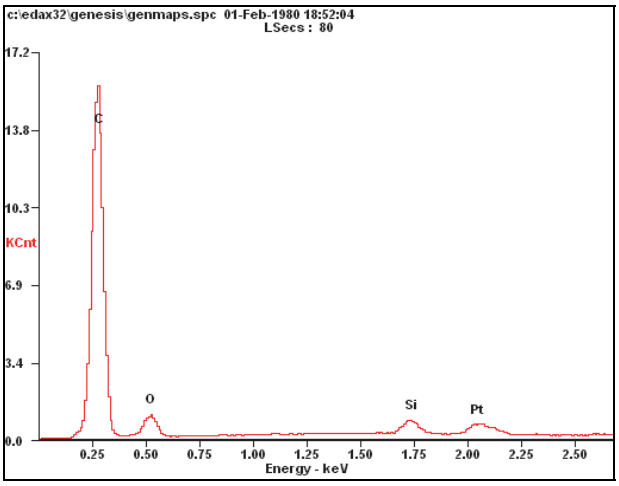
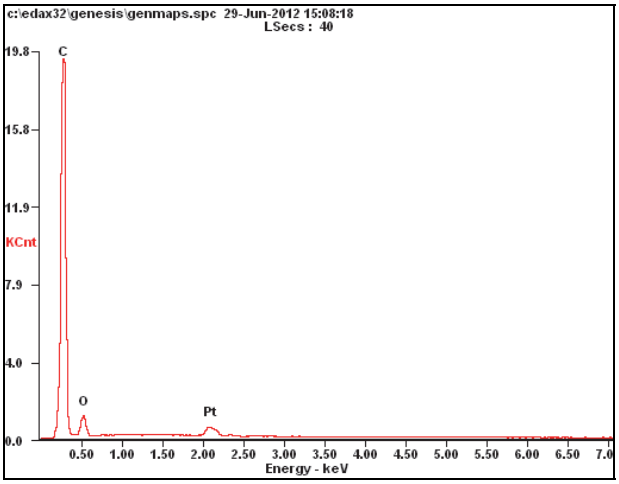


Figure S12. SEM image of 15 % - HMOCs. The hollow cavity is 130 nm. The scale is 1 µm.



Element	*Wt%*	*At%*
CK	86.56	90.11
OK	11.63	09.09
SiK	01.81	00.81
Matrix	Correction	ZAF

Figure S13. EDAX spectrum and analysis of 10 % - HMOCs without etching silica core.



Element	*Wt%*	*At%*
CK	91.24	93.28
OK	08.76	06.72
Matrix	Correction	ZAF

Figure S14. EDAX spectrum and analysis of 10 % - HMOCs.

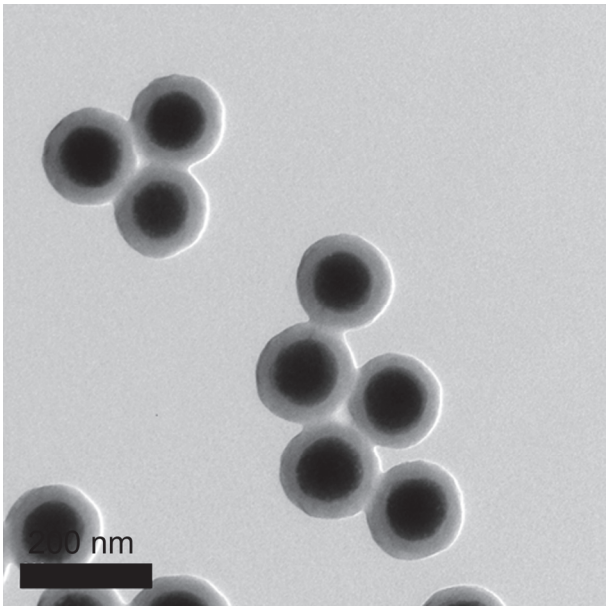


Figure S15. TEM image of 10 % - HMOCs - 2.5 ml. The SiO_2 nanoparticles core is 130 nm. The scale is 200 nm.

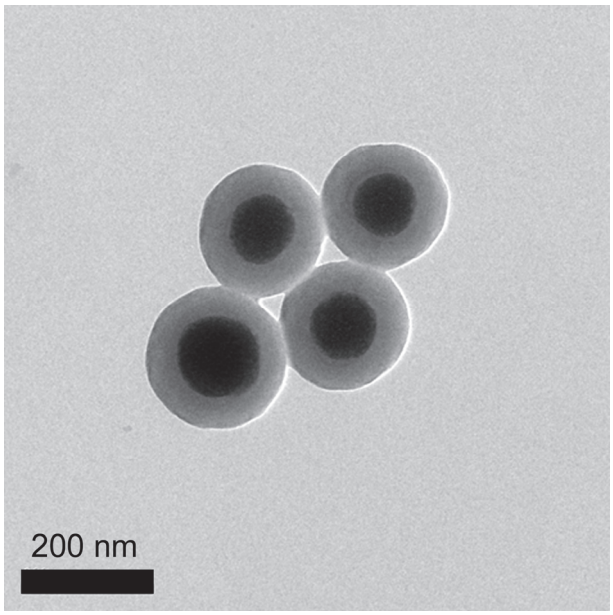


Figure S16. TEM image of 10 % - HMOCs - 5 ml. The SiO_2 nanoparticles core is 130 nm. The scale is 200 nm.

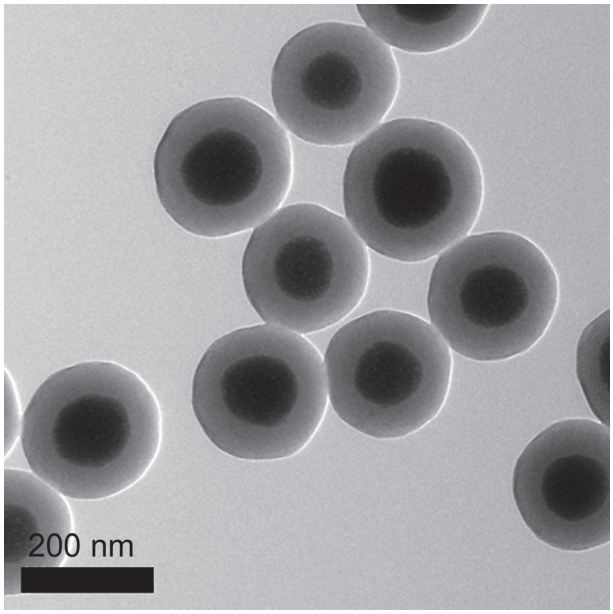


Figure S17. TEM image of 10 % - HMOCs - 10 ml. The SiO_2 nanoparticles core is 130 nm. The scale is 200 nm.

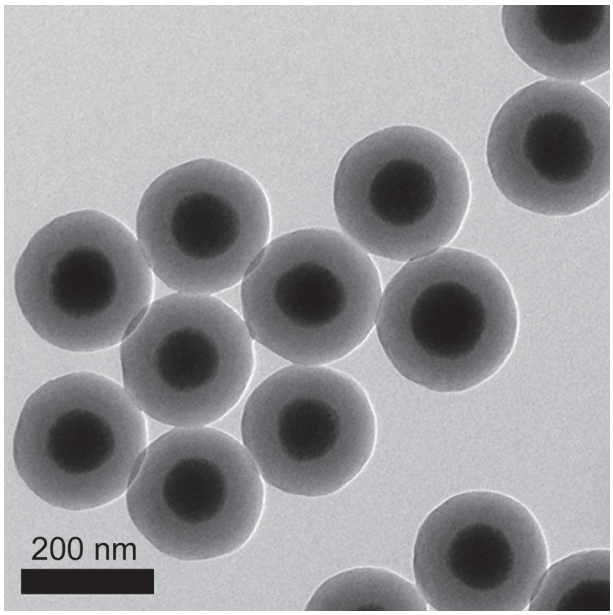


Figure S18. TEM image of 10 % - HMOCs - 15 ml. The SiO_2 nanoparticles core is 130 nm. The scale is 200 nm.

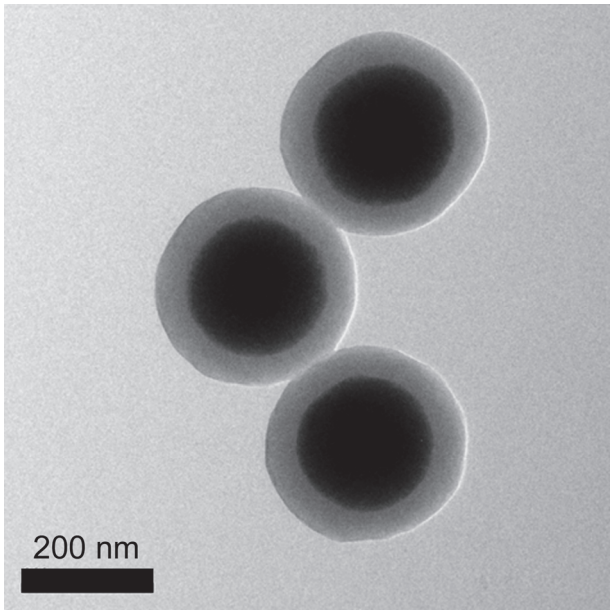


Figure S19. TEM image of 10 % - HMOCs - 5 ml – 200 nm. The SiO_2 nanoparticles core is 200 nm. The scale is 200 nm.

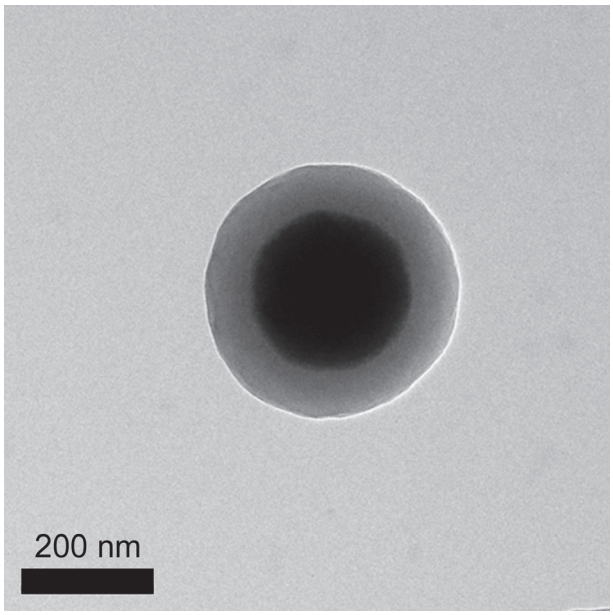


Figure S20. TEM image of 10 % - HMOCs - 10 ml – 200 nm. The SiO_2 nanoparticles core is 200 nm. The scale is 200 nm.

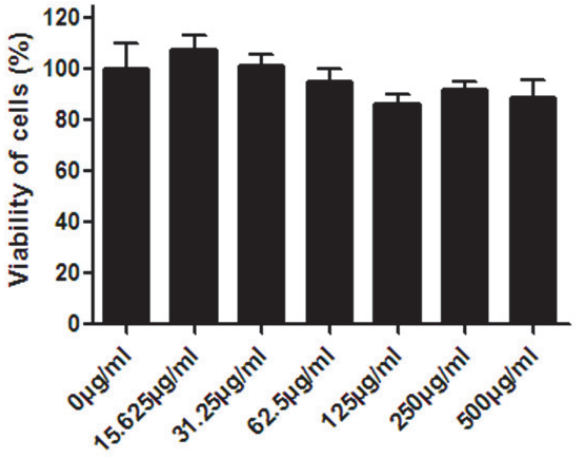


Figure S21. Cell viability measured using the MTT assays at concentrations that increase from left to right: 0, 15.6, 62.5, 125, 250 and 500 μg/mL.

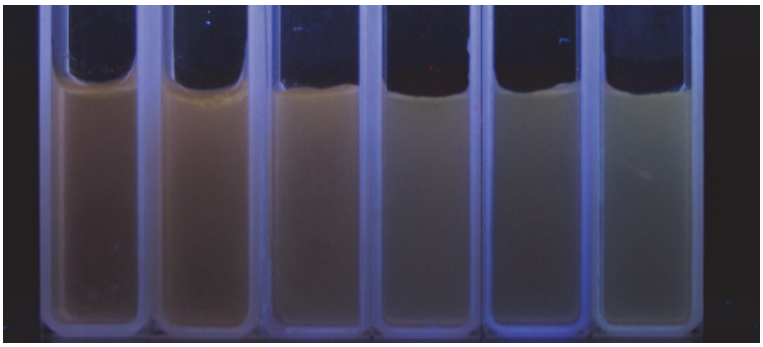


Figure S22. Optical images of 0.5 % - HMOCs to 15 % - HMOCs under a handy UV light at 365 nm. The blue light on the edge of colorimetric ware come from the blue light of handy UV light.

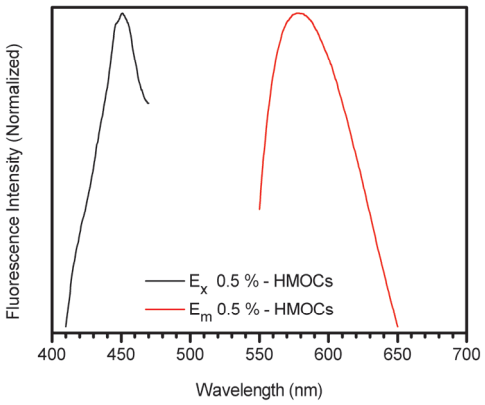


Figure S23. Fluorescence spectra of 0.5 % - HMOCs. Excitation spectra is black line and emission spectra is red line. The excitation wavelength is 440 nm.

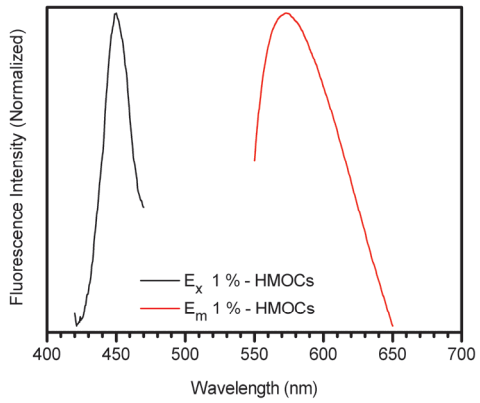


Figure S24. Fluorescence spectra of 1 % - HMOCs. Excitation spectra is black line and emission spectra is red line. The excitation wavelength is 440 nm.

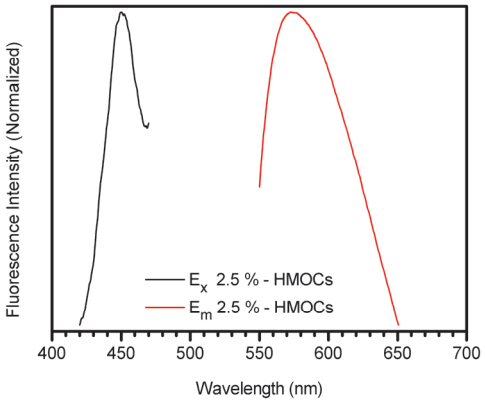


Figure S25. Fluorescence spectra of 2.5 % - HMOCs. Excitation spectra is black line and emission spectra is red line. The excitation wavelength is 440 nm.

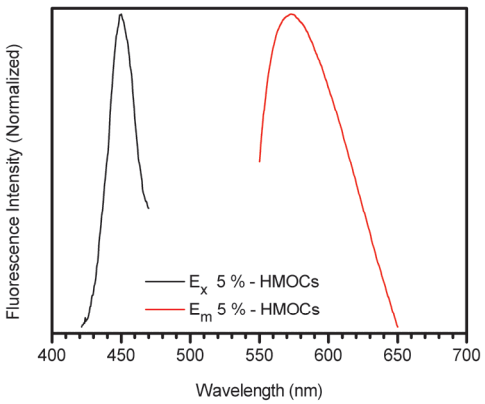


Figure S26. Fluorescence spectra of 5 % - HMOCs. Excitation spectra is black line and emission spectra is red line. The excitation wavelength is 440 nm.

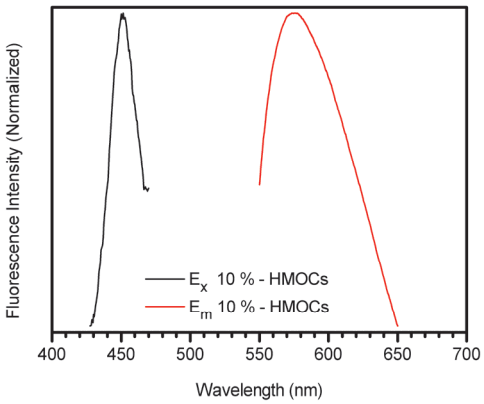


Figure S27. Fluorescence spectra of 10 % - HMOCs. Excitation spectra is black line and emission spectra is red line. The excitation wavelength is 440 nm.

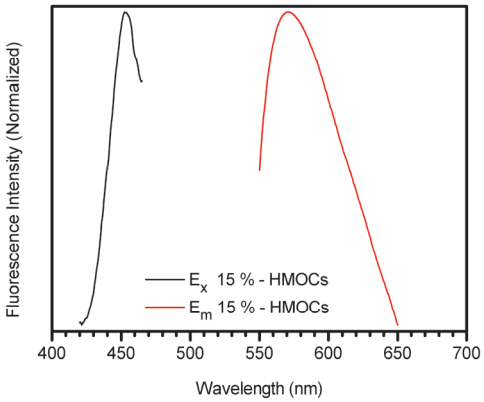


Figure S28. Fluorescence spectra of 15 % - HMOCs. Excitation spectra is black line and emission spectra is red line. The excitation wavelength is 440 nm.

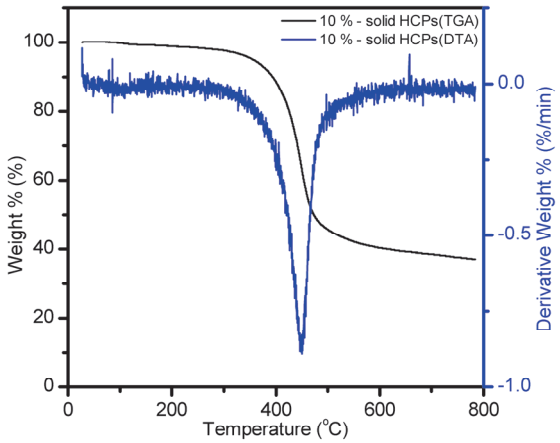


Figure S29. TGA and DTA under Nitrogen atmosphere of 10 % - solid HCPs without drug.

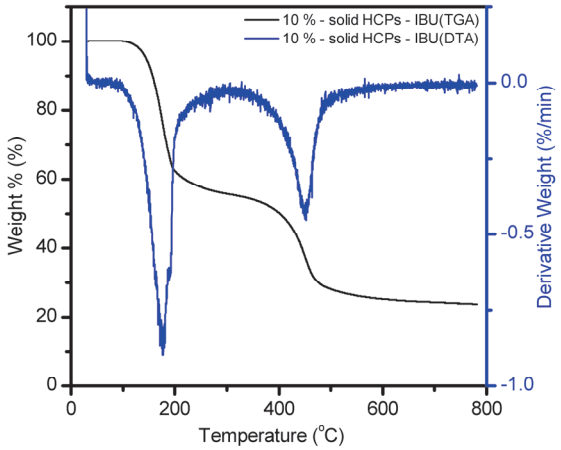


Figure S30. TGA and DTA under Nitrogen atmosphere of 10 % - solid HCPs with drug.

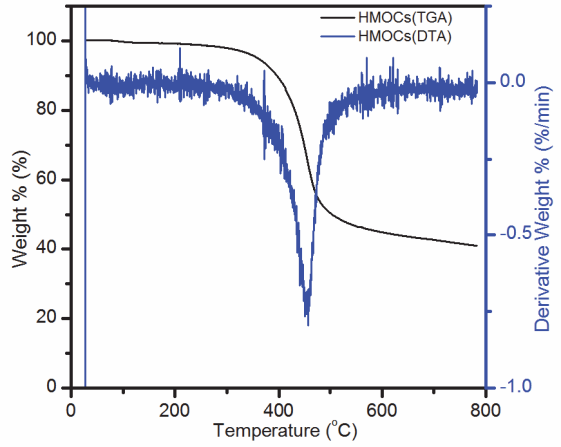


Figure S31. TGA and DTA under Nitrogen atmosphere of HMOCs without drug.

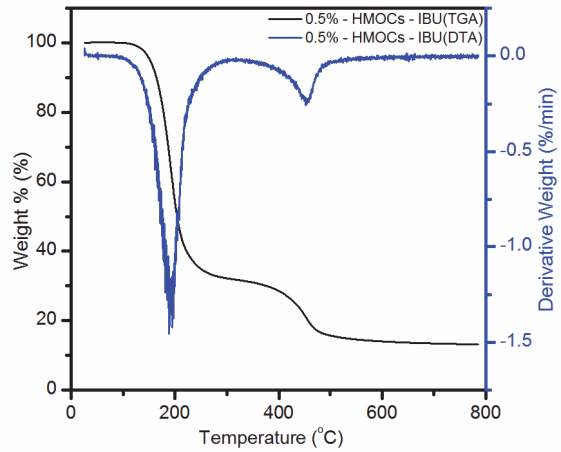


Figure S32. TGA and DTA under Nitrogen atmosphere of 0.5 % - HMOCs with drug.

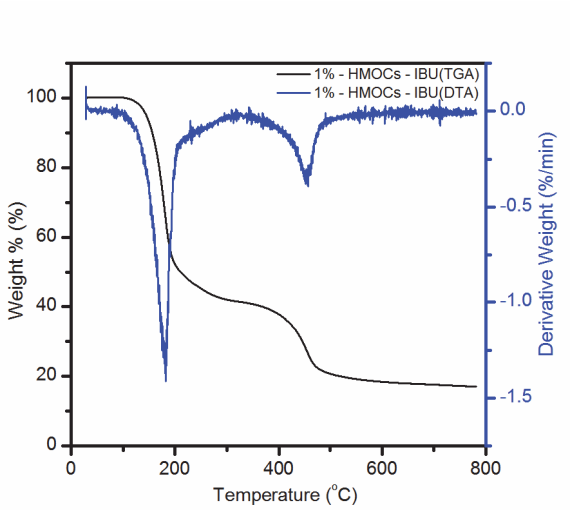


Figure S33. TGA and DTA under Nitrogen atmosphere of 1 % - HMOCs with drug.

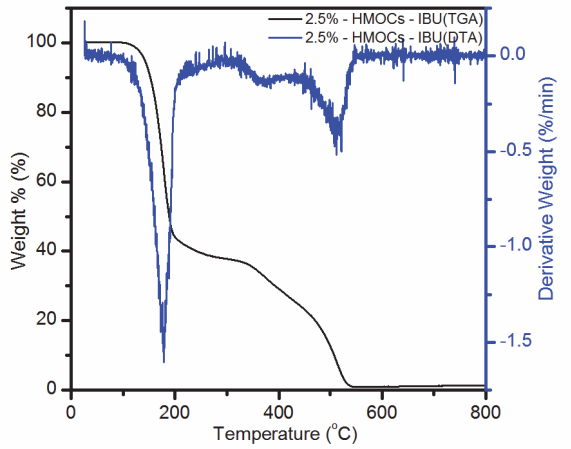


Figure S34. TGA and DTA under Nitrogen atmosphere of 2.5 % - HMOCs with drug.

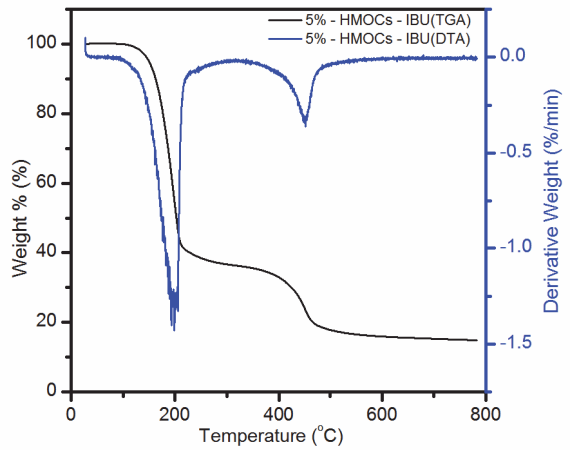


Figure S35. TGA and DTA under Nitrogen atmosphere of 5 % - HMOCs with drug.

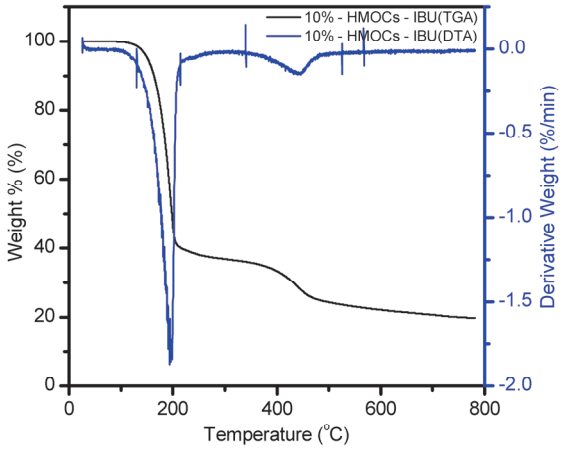


Figure S36. TGA and DTA under Nitrogen atmosphere of 10 % - HMOCs with drug.

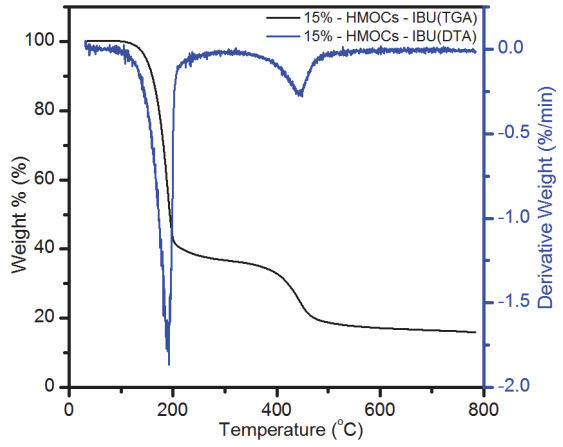


Figure S37. TGA and DTA under Nitrogen atmosphere of 15 % - HMOCs with drug.

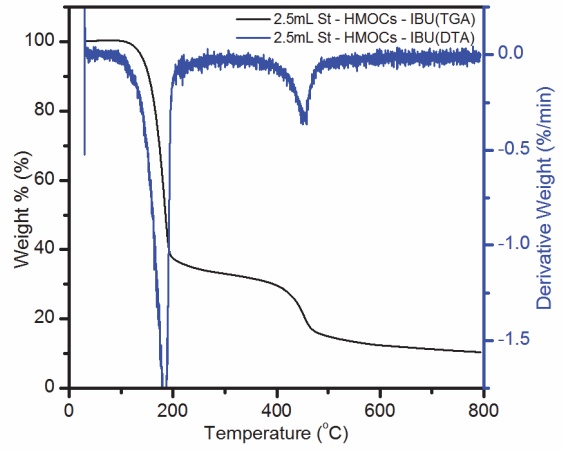


Figure S38. TGA and DTA under Nitrogen atmosphere of 10 % - HMOCs - 2.5 ml with drug.

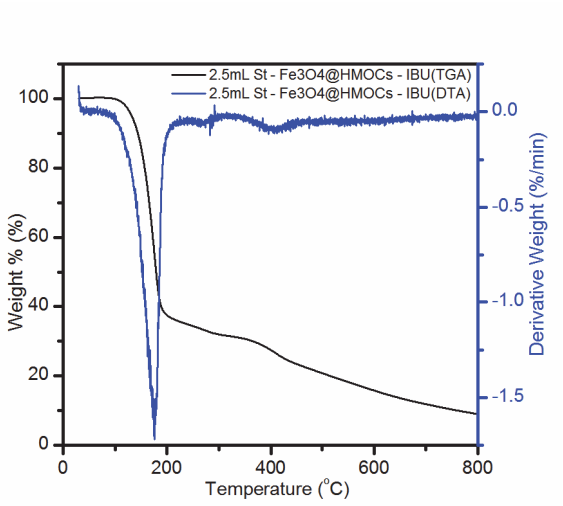


Figure S39. TGA and DTA under Nitrogen atmosphere of 10 % - HMOCs - 2.5 ml - Fe_3O_4 NPs with drug.

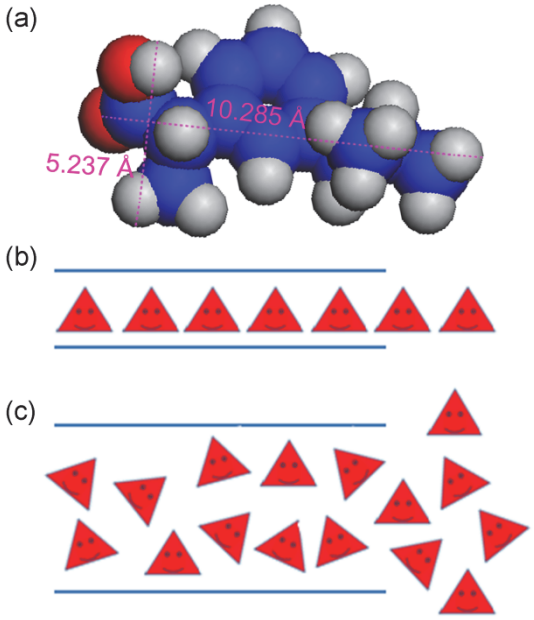


Figure S40. Simulated ibuprofen molecule; (a) schematic map of Ibuprofen molecule diffusion process in micropore (b) and mesopore (c).

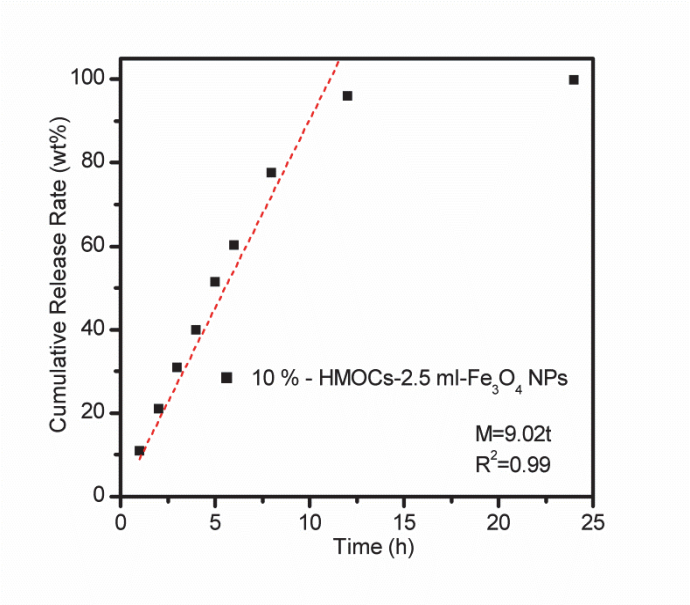


Figure S41. Drug release profile of 10 % - HMOCs - 2.5 ml - Fe_3O_4 NPs. The hollow is 130 nm. Red dash line is fitting line.

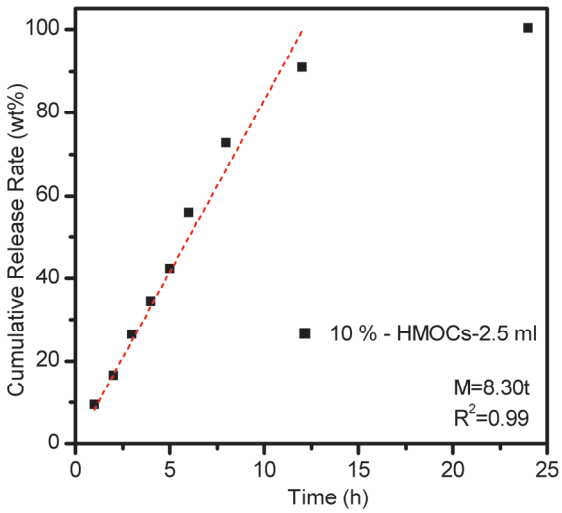


Figure S42. Drug release profile of 10 % - HMOCs - 2.5 ml. The hollow is 130 nm. Red dash line is fitting line.

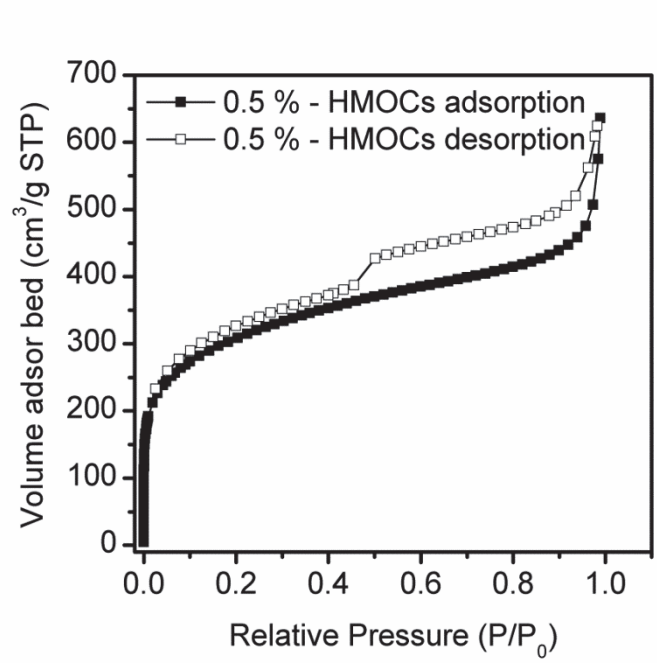


Figure S43. Nitrogen sorption and adsorption isotherms at 77.3 K of 0.5 % - HMOCs with 130 nm hollow cavity.

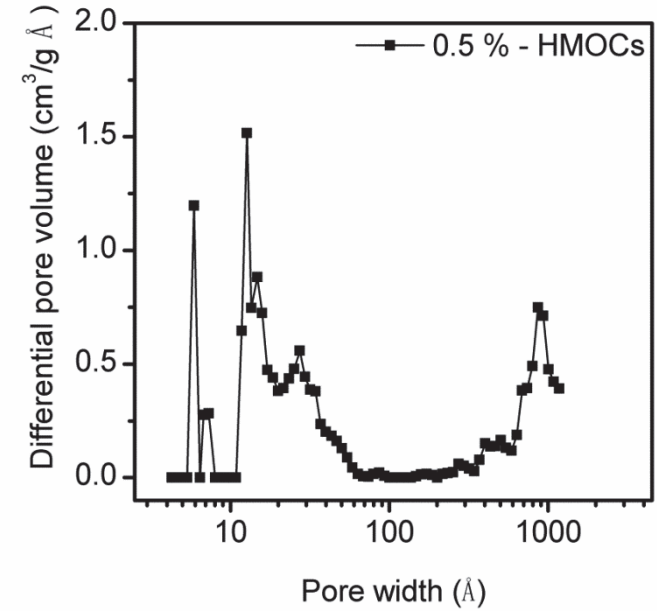


Figure S44. pore distribution of pore size calculated using DFT methods (slit pore models, differential pore volumes) of 0.5 % - HMOCs with 130 nm hollow cavity.

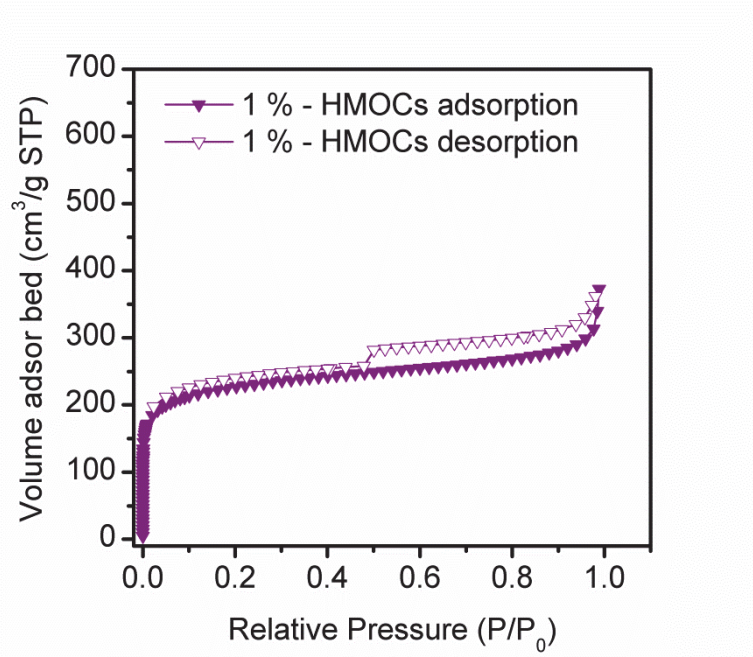


Figure S45. Nitrogen sorption and adsorption isotherms at 77.3 K of 1 % - HMOCs with 130 nm hollow cavity.

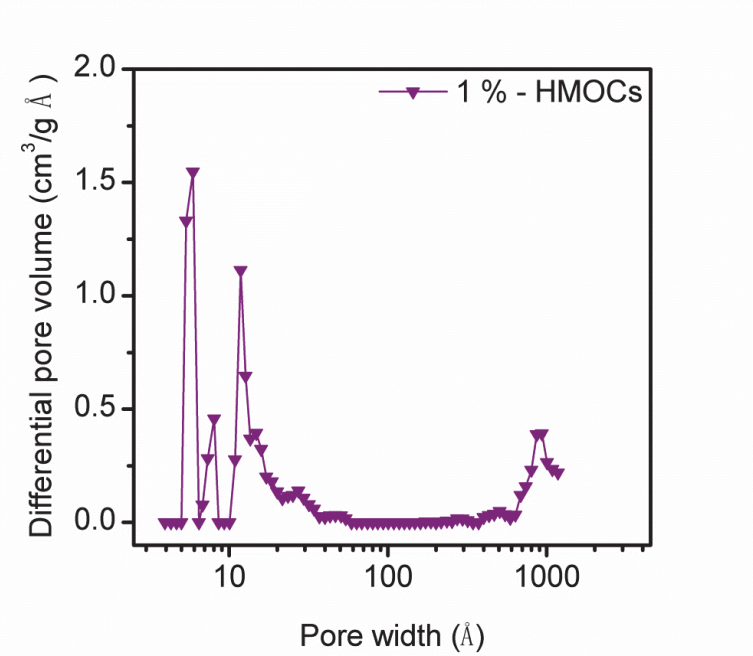


Figure S46. pore distribution of pore size calculated using DFT methods (slit pore models, differential pore volumes) of 1 % - HMOCs with 130 nm hollow cavity.

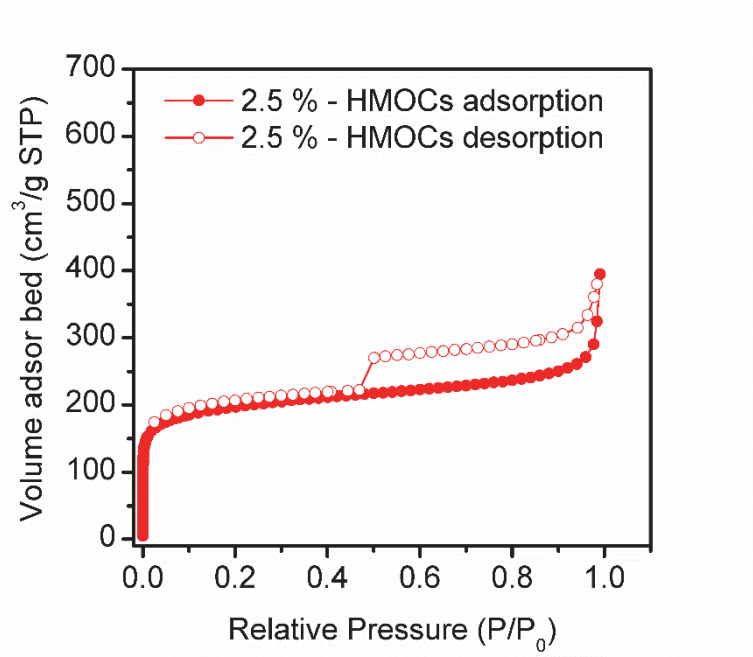


Figure S47. Nitrogen sorption and adsorption isotherms at 77.3 K of 2.5 % - HMOCs with 130 nm hollow cavity.

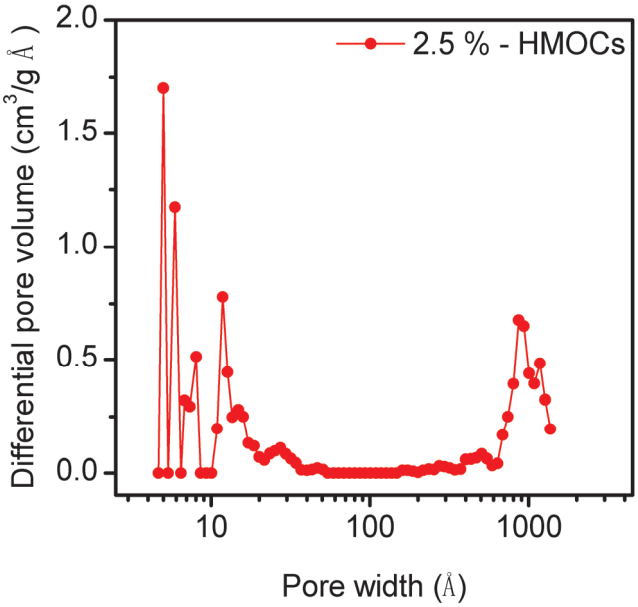


Figure S48. pore distribution of pore size calculated using DFT methods (slit pore models, differential pore volumes) of 2.5 % - HMOCs with 130 nm hollow cavity.

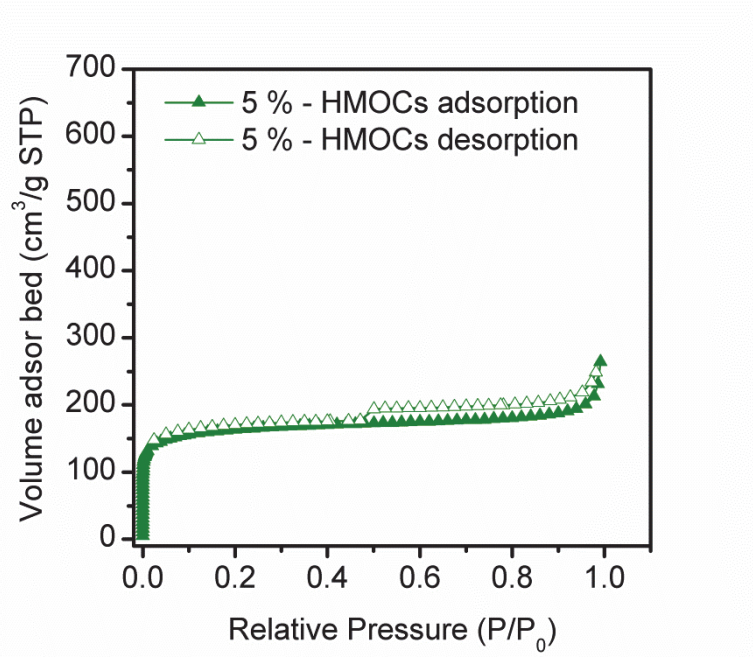


Figure S49. Nitrogen sorption and adsorption isotherms at 77.3 K of 5 % - HMOCs with 130 nm hollow cavity.

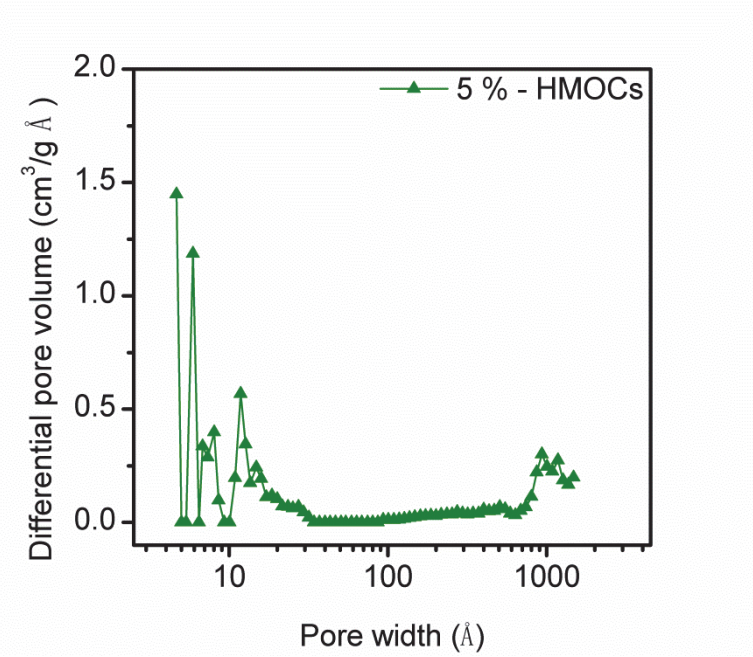


Figure S50. pore distribution of pore size calculated using DFT methods (slit pore models, differential pore volumes) of 5 % - HMOCs with 130 nm hollow cavity.

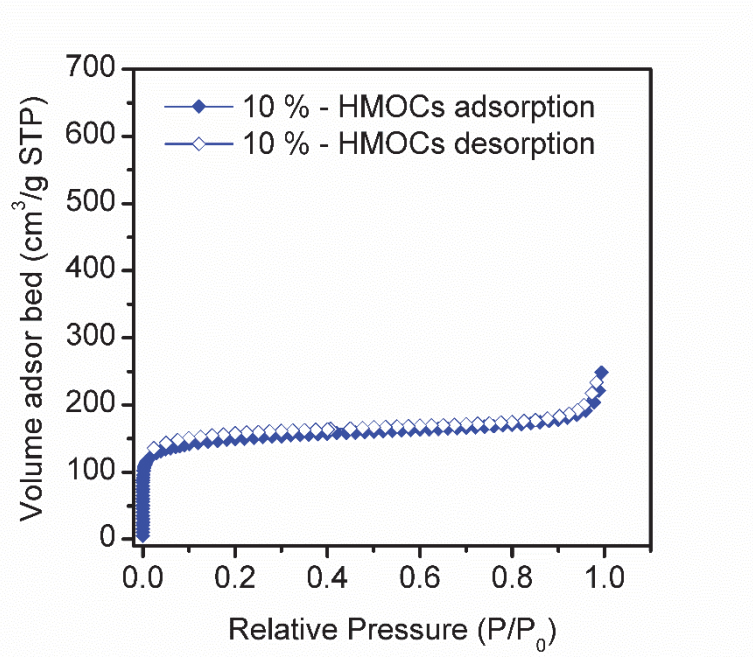


Figure S51. Nitrogen sorption and adsorption isotherms at 77.3 K of 10 % - HMOCs with 130 nm hollow cavity.

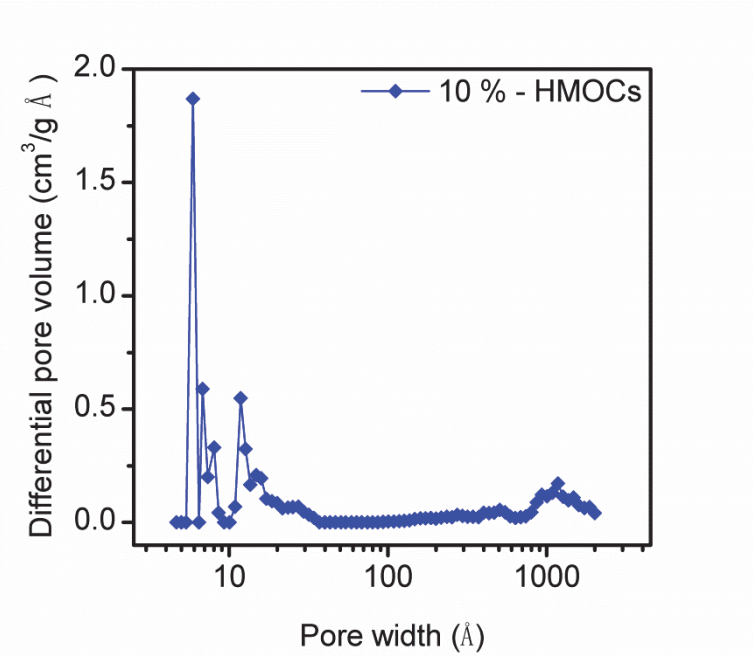


Figure S52. pore distribution of pore size calculated using DFT methods (slit pore models, differential pore volumes) of 10 % - HMOCs with 130 nm hollow cavity.

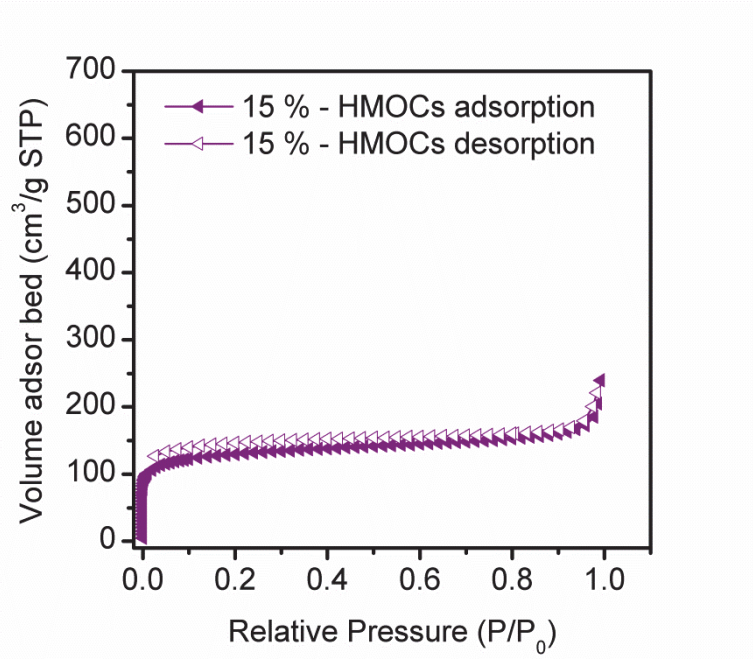


Figure S53. Nitrogen sorption and adsorption isotherms at 77.3 K of 15 % - HMOCs with 130 nm hollow cavity.

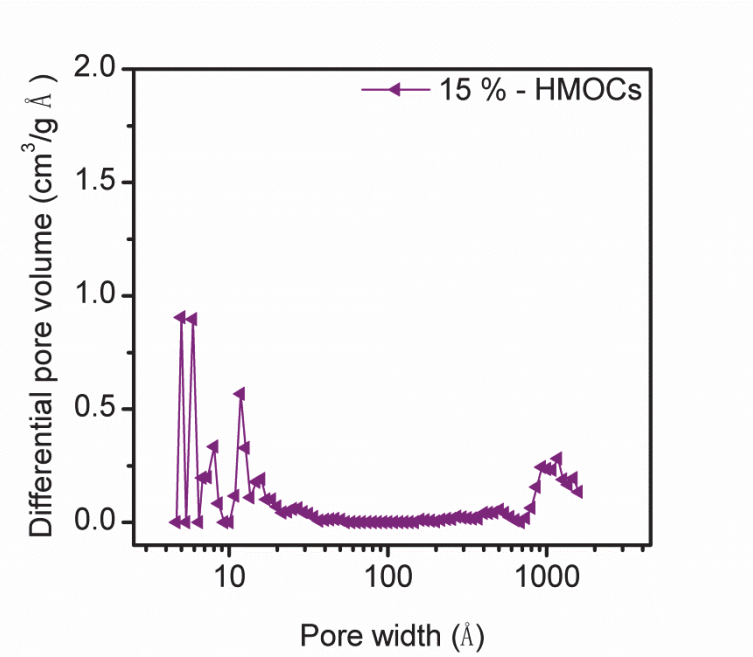


Figure S54. pore distribution of pore size calculated using DFT methods (slit pore models, differential pore volumes) of 15 % - HMOCs with 130 nm hollow cavity.

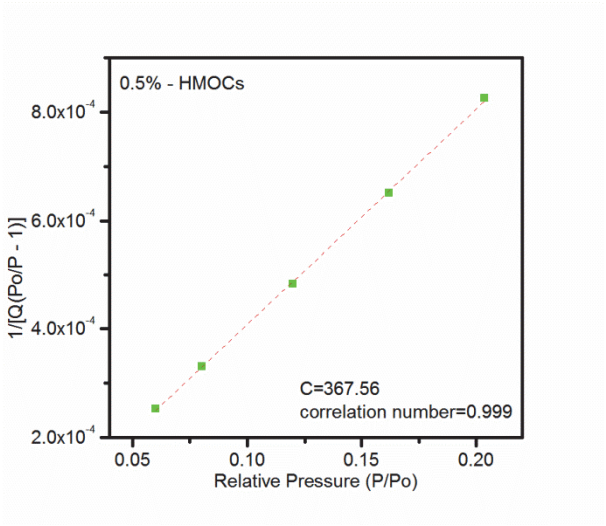


Figure S55. BET surface area plot of 0.5 % - HMOCs. The hollow is 130 nm. Red dash line is fitting line.

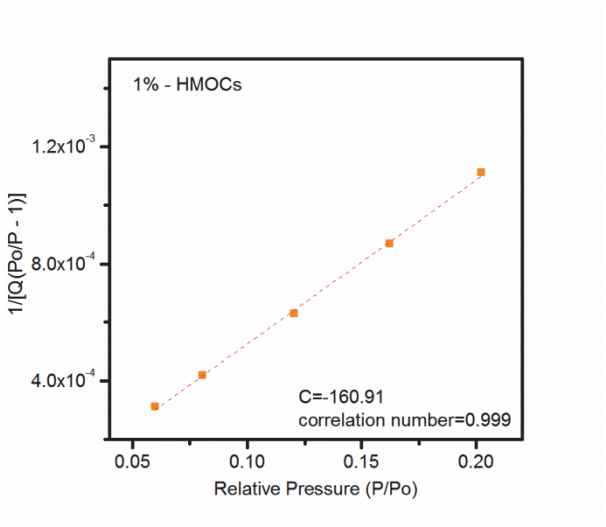


Figure S56. BET surface area plot of 1 % - HMOCs. The hollow is 130 nm. Red dash line is fitting line.

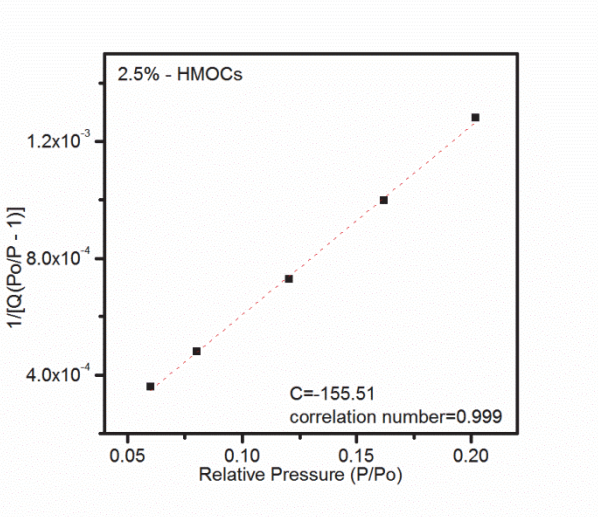


Figure S57. BET surface area plot of 2.5 % - HMOCs. The hollow is 130 nm. Red dash line is fitting line.

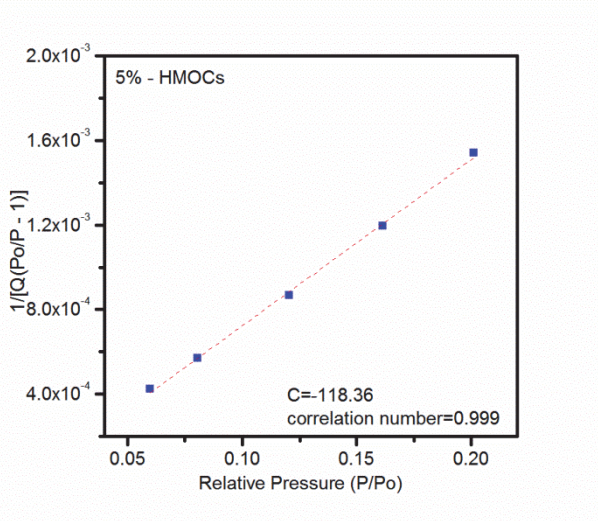


Figure S58. BET surface area plot of 5 % - HMOCs. The hollow is 130 nm. Red dash line is fitting line.

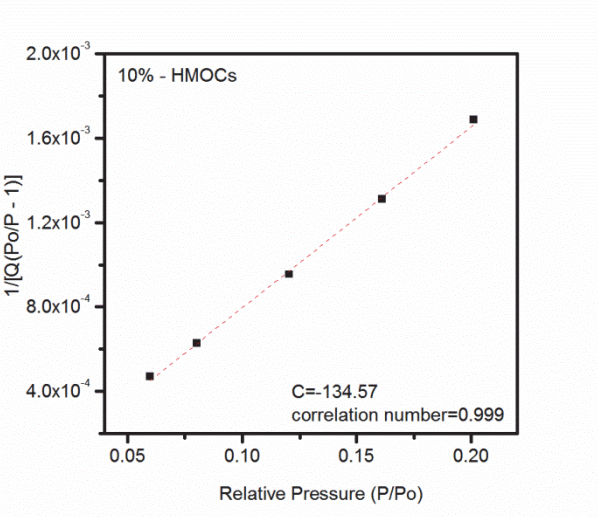


Figure S59. BET surface area plot of 10 % - HMOCs. The hollow is 130 nm. Red dash line is fitting line.

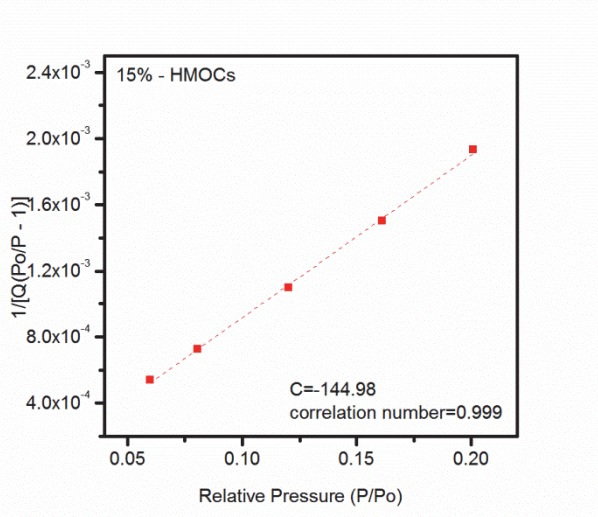


Figure S60. BET surface area plot of 15 % - HMOCs. The hollow is 130 nm. Red dash line is fitting line.

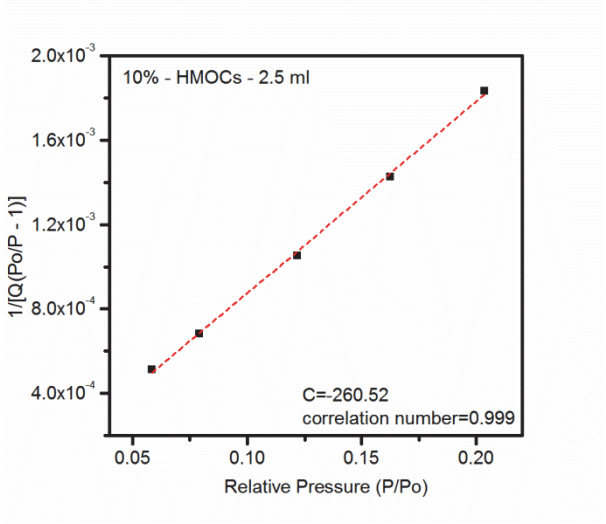


Figure S61. BET surface area plot of 10 % - HMOCs – 2.5 ml. The hollow is 130 nm. Red dash line is fitting line.

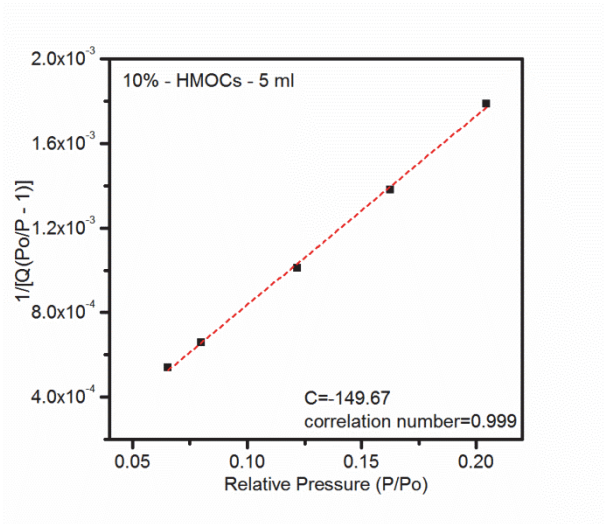


Figure S62. BET surface area plot of 10 % - HMOCs – 5 ml. The hollow is 130 nm. Red dash line is fitting line.

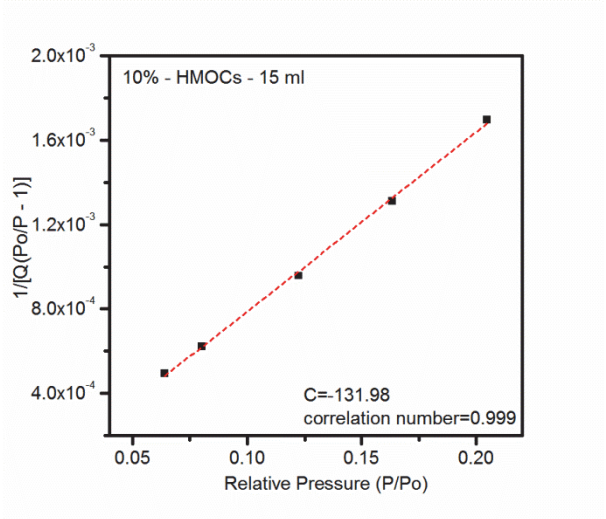


Figure S63. BET surface area plot of 10 % - HMOCs – 15 ml. The hollow is 130 nm. Red dash line is fitting line.

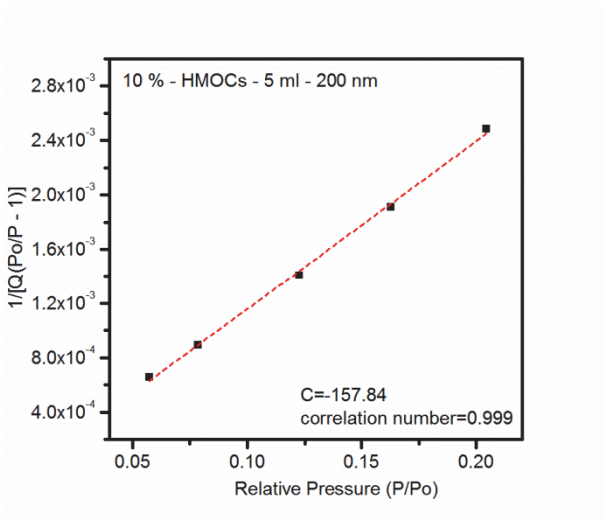


Figure S64. BET surface area plot of 10 % - HMOCs – 5 ml – 200nm. The hollow is 200 nm. Red dash line is fitting line.

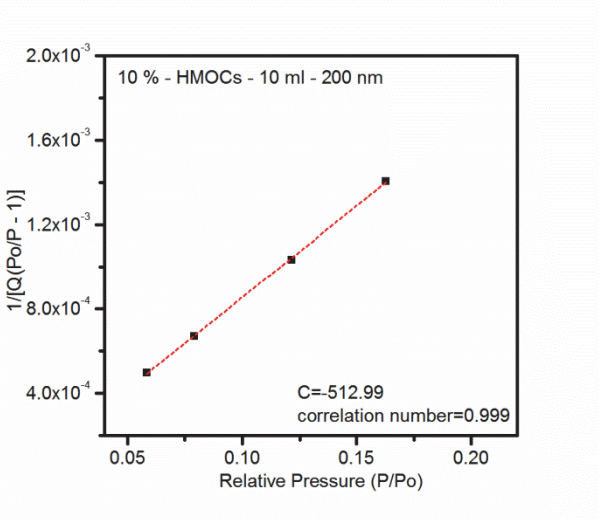


Figure S65. BET surface area plot of 10 % - HMOCs – 10 ml – 200nm. The hollow is 200 nm. Red dash line is fitting line.

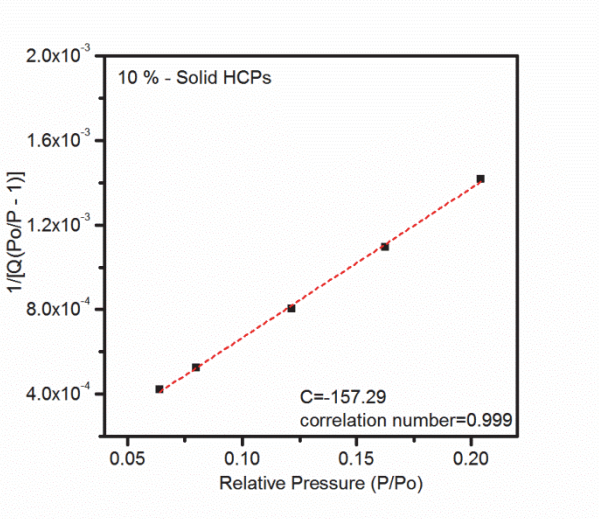


Figure S66. BET surface area plot of 10 % - Solid HCPs. Red dash line is fitting line.

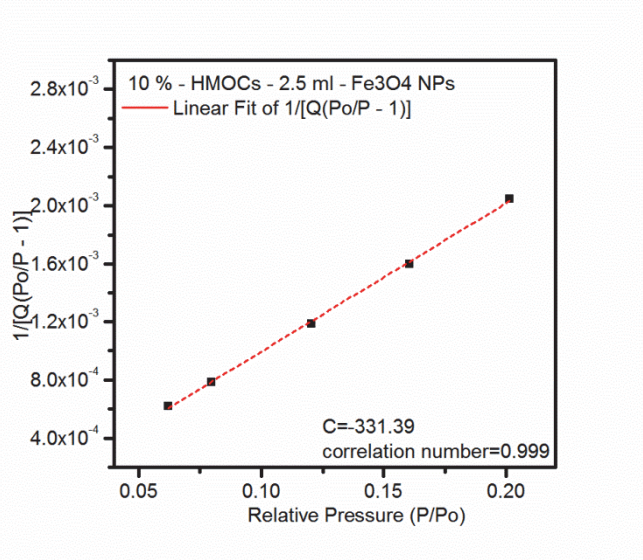


Figure S67. BET surface area plot of 10 % - HMOCs - 2.5 ml - Fe_3O_4 NPs. The hollow is 130 nm. Red dash line is fitting line.

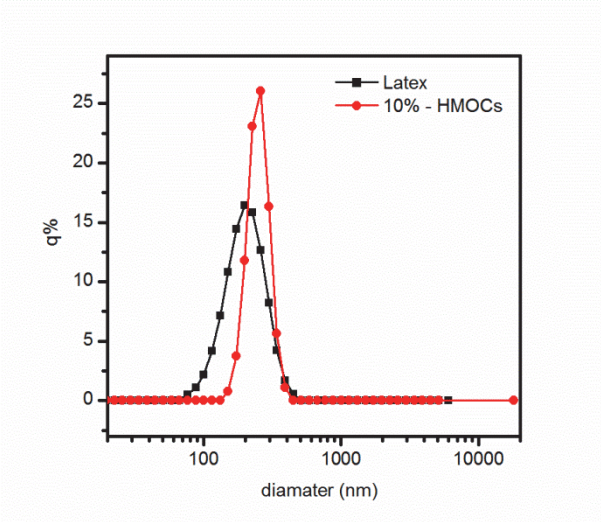


Figure S68. Dynamic light scattering of latex (black) and 10 % - HMOCs (red).

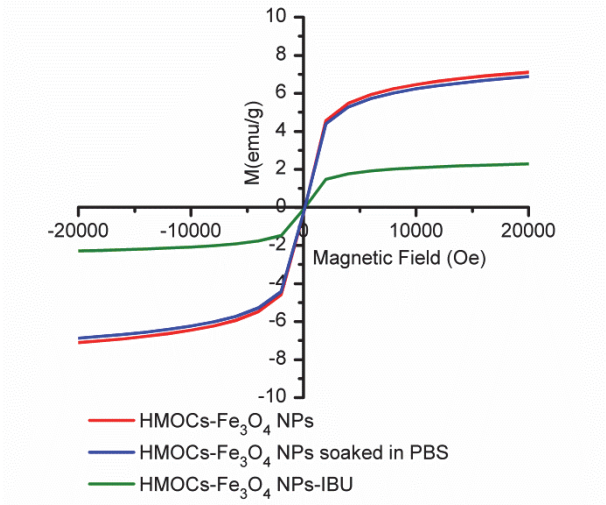


Figure S69. 300 K magnified magnetization isotherms of 10 % - HMOCs - 2.5 ml - Fe_3O_4 NPs, (red line) 10 % - HMOCs - 2.5 ml - Fe_3O_4 NPs after soaked in PBS for 48 h (blue line) and 10 % - HMOCs - 2.5 ml - Fe_3O_4 NPs loaded with drug (green line).

Table S1. Surface area and porosity of HMOCs.

Samples	Hollow cavity	St	DVB	S_{BET} [a]	S_L [b]	PV [d]
	nm	ml	%	m^2/g	m^2/g	cm^3/g
0.5 % - HMOCs	130	10	0.5	1129	1549	0.98
1 % - HMOCs	130	10	1	815	1098	0.61
2.5 % - HMOCs	130	10	2.5	697	932	0.59
5 % - HMOCs	130	10	5	589	788	0.42
10 % - HMOCs	130	10	10	516	691	0.35
15 % - HMOCs	130	10	15	478	640	0.35
10 % - HMOCs - 2.5 ml	130	2.5	10	480	645	0.45
10 % - HMOCs - 5 ml	130	5	10	489	658	0.40
10 % - HMOCs - 15 ml	130	15	10	514	690	0.38
10 % - HMOCs - 5 ml - 200 nm	200	5	10	354	473	0.23
10 % - HMOCs - 10 ml - 200 nm	200	10	10	500	640	0.36
10 % - Solid HCPs	/	10	10	616	829	0.83
10 % - HMOCs - 2.5 ml - Fe_3O_4 NPs;	130	2.5	10	426	573	0.54

[a] Surface area calculated from nitrogen adsorption isotherms at 77.3 K using BET equation.

[b] Surface area calculated from nitrogen adsorption isotherms at 77.3 K using Langmuir equation.

[c] Micropore volume determined from the N_2 isotherm at $P/P_0 = 0.050$

[d] Pore volume calculated from nitrogen isotherm at P/P_0=0.995, 77.3 K.

Table S2. Drug upload

Samples	Drug Upload [a] ibuprofen/g	Drug Upload [b] ibuprofen/g	Average Drug Upload [c] ibuprofen/g
0.5 % - HMOCs	1.97	2.12	2.04
1 % - HMOCs	1.92	1.44	1.68
2.5 % - HMOCs	2.00	1.64	1.82
5 % - HMOCs	1.90	1.68	1.79
10 % - HMOCs	1.85	1.72	1.78
15 % - HMOCs	1.77	1.73	1.75
10% - solid HCPs	0.84	0.76	0.80
10 % - HMOCs-2.5 ml	2.15	1.97	2.06
10 % - HMOCs-2.5 ml-Fe_3O_4 NPs	2.14	1.95	2.04

[a] Drug uptake calculated by UV data.

[b] Drug uptake calculated by TG data.

[c] Average of a and b.