A highly porous medical metal-organic framework constructed from bioactive curcumin

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1. General experimental procedures

Materials: Curcumin (Sinopharm Chemical reagent Co.Ltd, AR), Zinc acetate dehydrate ($Zn(OAc)_2 \cdot 2H_2O$, AR), *N,N'*-dimethylacetamide (Tianjin Tiantai Chemical Research Institute, AR), and absolute ethanol (Beijing Chemical Company, AR) were used as received without any further purification.

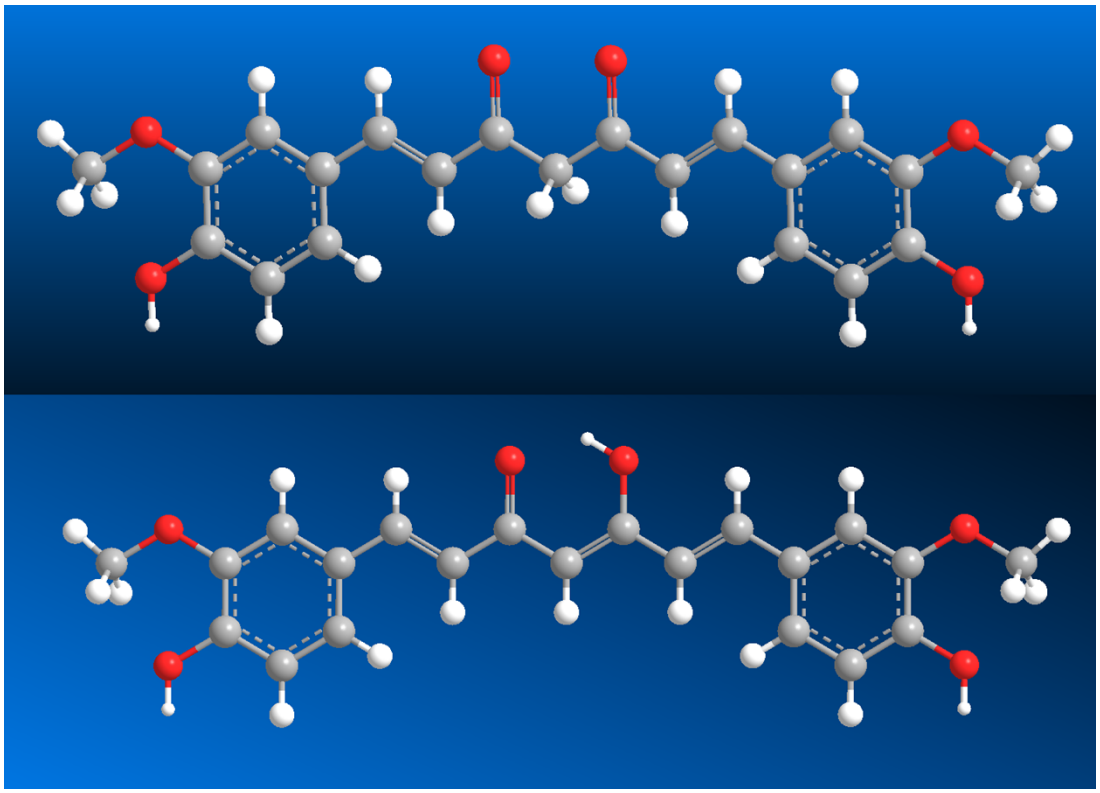

Fig. S1 The tautomeric forms of curcumin: 1,3-diketo form (top) and enol forms (bottom, one of two equivalent forms).

Characterizations: Powder X-ray diffraction (PXRD) was collected on a Rigaku D/Max 2550 X-ray diffractometer with Cu-Kα radiation (λ=1.5418 Å) at 50 kV, 20 mA with a scanning rate of 6°/min and a step size of 0.02°. The simulated powder patterns were calculated using Mercury 2.0. The purity and homogeneity of the bulk products were determined by comparison of the simulated and experimental X-ray powder diffraction patterns. Fourier transform infrared (FT-IR) spectra were measured using a Nicolet Impact 410 FTIR spectrometer in the range of 400-4000 cm^{-1} and KBr pellet samples. Absorptions are described as follows: very strong (vs), strong(s), medium (m), weak (w), shoulder (sh), and broad (br). The elemental

analyses data was carried out on vario MICRO CHN element analyzer. Thermogravimetric analysis was performed under air atmosphere from room temperature to 800 °C at a heating ramp of 10 °C min^{-1}, using a Perkin-Elmer TGA 7 thermogravimetric analyzer. The N_2 adsorption and desorption isotherms were measured on Autosorb iQ_2 adsorptometer, Quantachrome Instruments. Adsorption isotherms were measured at 77 K in a liquid nitrogen bath. Correlation coefficient of medi-MOF-1 surface area values is 0.999997, C constant is 2715.244. The as-synthesized medi-MOF-1 solids were firstly treated in CH_2Cl_2 for 24 h (3 times) for the N_2 sorption measurements. The solids were treated at 100 °C under vacuum for 8 h before the measurement. The medi-MOF-1 and the Ibuprofen-loaded sample were weighed and transferred to bulb cells of 9 mm in diameter. Medi-MOF-1 was entirely desolvated under vacuum overnight at 100 °C, and the Ibuprofen-loaded samples at 65 °C to avoid the degradation of drug molecules.

Synthesis of medi-MOF-1: Curcumin (60 mg, 0.1629 mmol) and $Zn(OAc)_2 \cdot 2H_2O$ (20 mg, 0.0911 mmol) were added to a mixed solvent of *N,N'*-dimethylacetamide (4.0 mL) and absolute ethanol (1.0 mL). After stirring at room temperature for 4 h, the solution was heated in closed vessel at 75 °C for 3 days to obtain red crystals with a size at about 300 μm. The crystals were collected, and then washed with DMF (3×5 mL), and dried under air (yield: 85%). ***Elemental analysis***: $C_{76}H_{115}N_7Zn_3O_{22}$ $=Zn_3(C_{21}H_{17}O_6)_2$, 7DMA and $3C_2H_5OH$. Calcd. C, 54.49; H, 6.92; N, 5.85. Found C, 53.88; H, 6.141; N, 5.85. ***FT-IR***: (KBr 4000-400 cm^{-1}) 3510(br), 3035(br), 2937(br), 2832(w), 2610(w), 1622(m), 1593(m), 1502(s), 1463(sh), 1400(m), 1280(s), 1223(m), 1157(m), 1124(m), 1027(m), 968(s), 840(m), 819(s), 765(w), 729(w), 628(sh), 603(w), 561(m), 467(m).

Stability of medi-MOF-1:

Thermostability: 10 mg of medi-MOF-1 was heated from 200 °C to 350 °C at a 50 °C temperature gradient to text its stability.

Stability in some solvents: 10 mg of medi-MOF-1 was respectively immersed in absolute ethanol, CH_2Cl_2, n-hexane, PBS and water at room temperature for three

days.

Samples stability were detected by Powder X-ray diffraction as shown in Fig. S10 and Fig. S11

2. Crystallographic data and structure

Suitable single crystal of medi-MOF-1 was mounted on a Bruker SMART APEX CCD diffractometer using graphite-monochromated Mo Kα (λ = 0.71073 Å) radiation. Data collection was performed using φ and ω scans. An empirical absorption correction was applied to the collected data using the SADABS program. The structures were solved using direct methods (SHELXS) which located the position of most of the non-hydrogen atoms. The structure were treated by full matrix least-squares refinement against F^2 (all data HKLF 4 format) using SHELXTL. Subsequent difference Fourier synthesis and least-squares refinement revealed the positions of the remaining non-hydrogen atoms. All non-hydrogen atoms were refined with independent anisotropic displacement parameters, and all the hydrogen atoms were fixed at calculated positions and refined by using a riding mode. All the calculations and graphics were carried out using SHELX-2013, PLATON, ORTEP-3, CIFTAB, MERCURY within WinGX system, version 2013.3. The parameters used during the collection of diffraction data are summarized in Table S1.

Final difference Fourier syntheses showed only chemically insignificant electron density (largest difference peak 0.78 Å). However, there is evidence of considerable solvent in the structure. Calculations using SQUEEZE/PLATION show total potential solvent accessible void volume of 4710.6 $Å^3$ (out of 7000.2 $Å^3$ unit cell volume) with 1285 e^- per void volume per unit cell.

Table S1. Crystal data and structure refinement for medi-MOF-1.

Identification code	medi-MOF-1	
Empirical formula	C42 H34 O12 Zn3	
Formula weight	926.86	
Temperature	293(2) K	
Wavelength	0.71073 Å	
Crystal system	Trigonal	
Space group	$P3_221$	
Unit cell dimensions	a = 18.1019(8) Å	α= 90°.
	b = 18.1019(8) Å	β= 90°.
	c = 24.668(2) Å	γ = 120°.
Volume	7000.2(7) $Å^3$	
Z	3	
Density (calculated)	0.660 Mg/m^3	
Absorption coefficient	0.792 mm^{-1}	
F(000)	1416	
Crystal size	0.40 x 0.30 x 0.20 mm^3	
Theta range for data collection	1.30 to 25.49°.	
Index ranges	-21<=h<=21, -14<=k<=21, -26<=l<=29	
Reflections collected	36843	
Independent reflections	8651 [R(int) = 0.1176]	
Completeness to theta = 25.49°	99.8 %	
Max. and min. transmission	0.854 and 0.752	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	8651 / 0 / 261	
Goodness-of-fit on F^2	1.078	
Final R indices [I>2sigma(I)]	R1 = 0.0692, wR2 = 0.2338	
R indices (all data)	R1 = 0.1335, wR2 = 0.2569	
Absolute structure parameter	0.52(3)	
Largest diff. peak and hole	0.764 and -0.584 $e.Å^{-3}$	

Table S2. Atomic coordinates (× 10^4) and equivalent isotropic displacement parameters (Å^2× 10^3) for medi-MOF-1. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
C(1)	3848(13)	5241(9)	10309(5)	160(9)
C(2)	3725(6)	4219(6)	9022(3)	51(2)
C(3)	3966(6)	4886(6)	9396(3)	56(3)
C(4)	4450(7)	5732(6)	9247(4)	70(3)
C(5)	4714(8)	5923(6)	8687(4)	77(3)
C(6)	4422(9)	5276(7)	8325(4)	91(4)
C(7)	3945(7)	4416(7)	8482(3)	72(3)
C(8)	5299(7)	6799(7)	8509(4)	83(4)
C(9)	5789(8)	7483(7)	8831(4)	80(4)
C(10)	6399(6)	8319(6)	8623(3)	52(3)
C(11)	7001(7)	8883(6)	8956(4)	63(3)
C(12)	7728(6)	9675(7)	8825(3)	53(2)
C(13)	8383(7)	10157(6)	9236(3)	60(3)
C(14)	9109(6)	10869(7)	9104(4)	60(3)
C(15)	9830(6)	11391(6)	9446(3)	52(3)
C(16)	10505(6)	12086(7)	9205(4)	63(3)
C(17)	11252(7)	12629(7)	9485(4)	65(3)
C(18)	11359(6)	12448(6)	10023(3)	48(2)
C(19)	10671(6)	11752(6)	10276(3)	51(3)
C(20)	9918(6)	11232(6)	9992(4)	57(3)
C(21)	10230(7)	10904(8)	11090(4)	85(4)
O(1)	3692(5)	4630(4)	9915(2)	73(2)
O(2)	3295(4)	3425(4)	9209(2)	50(1)
O(3)	6351(4)	8413(4)	8119(2)	62(2)
O(4)	7893(4)	10003(4)	8350(2)	49(2)
O(5)	12072(4)	12916(4)	10288(2)	48(2)
O(6)	10829(4)	11649(4)	10801(2)	61(2)
Zn(1)	3242(1)	3242(1)	10000	47(1)
Zn(2)	2805(1)	2220(1)	8937(1)	44(1)

Table S3. Bond lengths [Å] and angles [°] for medi-MOF-1.

C(1)-O(2)	1.391(13)	C(18)-O(5)	1.309(10)
C(1)-H(1A)	0.9600	C(18)-C(19)	1.398(12)
C(1)-H(1B)	0.9600	C(19)-O(6)	1.360(10)
C(1)-H(1C)	0.9600	C(19)-C(20)	1.396(12)
C(2)-O(2)	1.328(10)	C(20)-H(20)	0.9300
C(2)-C(7)	1.384(11)	C(21)-O(6)	1.428(12)
C(2)-C(3)	1.406(12)	C(21)-H(21A)	0.9600
C(3)-O(1)	1.367(10)	C(21)-H(21B)	0.9600
C(3)-C(4)	1.381(12)	C(21)-H(21C)	0.9600
C(4)-C(5)	1.446(12)	O(1)-Zn(1)	2.229(6)
C(4)-H(4)	0.9300	O(2)-Zn(1)	1.974(5)
C(5)-C(6)	1.352(13)	O(2)-Zn(2)	2.014(6)
C(5)-C(8)	1.465(13)	O(3)-Zn(2)#1	1.944(6)
C(6)-C(7)	1.406(14)	O(4)-Zn(2) #1	1.931(6)
C(6)-H(6)	0.9300	O(5)-Zn(2)#2	1.954(5)
C(7)-H(7)	0.9300	O(5)-Zn(1)#3	2.023(6)
C(8)-C(9)	1.362(14)	O(6)-Zn(2)#2	2.423(6)
C(8)-H(8)	0.9300	Zn(1)-O(2)#4	1.974(5)
C(9)-C(10)	1.449(13)	Zn(1)-O(5)#5	2.023(6)
C(9)-H(9)	0.9300	Zn(1)-O(5)#6	2.023(6)
C(10)-O(3)	1.264(9)	Zn(1)-Zn(1)#4	2.229(6)
C(10)-C(11)	1.339(12)	Zn(1)-Zn(2)#4	3.0748(11)
C(11)-C(12)	1.416(13)	Zn(2)-Zn(4)#7	1.931(6)
C(11)-H(11)	0.9300	Zn(2)-Zn(3)#7	1.944(6)
C(12)-O(4)	1.279(10)	Zn(2)-Zn(5)#6	1.954(5)
C(12)-C(13)	1.470(12)	Zn(2)-Zn(6)#6	2.423(6)
C(13)-C(14)	1.342(13)		
C(13)-H(13)	0.9300	O(1)-C(1)-H(1A)	109.5
C(14)-C(15)	1.441(13)	O(1)-C(1)-H(1B)	109.5
C(14)-H(14)	0.9300	H(1A)-C(1)-H(1B)	109.5
C(15)-C(16)	1.377(13)	O(1)-C(1)-H(1C)	109.5
C(15)-C(20)	1.402(12)	H(1A)-C(1)-H(1C)	109.5
C(16)-C(17)	1.394(13)	H(1B)-C(1)-H(1C)	109.5
C(16)-H(16)	0.9300	O(2)-C(2)-C(7)	123.4(8)
C(17)-C(18)	1.404(11)	O(2)-C(2)-C(3)	117.6(7)
C(17)-H(17)	0.9300	C(7)-C(2)-C(3)	119.0(9)

O(1)-C(3)-C(4)	123.2(8)	C(15)-C(16)-C(17)	122.3(8)
O(1)-C(3)-C(2)	114.8(8)	C(15)-C(16)-H(16)	118.9
C(4)-C(3)-C(2)	122.0(8)	C(17)-C(16)-H(16)	118.9
C(3)-C(4)-C(5)	118.0(9)	C(16)-C(17)-C(18)	120.3(9)
C(3)-C(4)-H(4)	121.0	C(16)-C(17)-H(17)	119.9
C(5)-C(4)-H(4)	121.0	C(18)-C(17)-H(17)	119.9
C(6)-C(5)-C(8)	119.8(10)	O(5)-C(18)-C(19)	120.5(8)
C(4)-C(5)-C(8)	121.1(9)	O(5)-C(18)-C(17)	121.8(8)
C(5)-C(6)-C(7)	122.2(9)	C(19)-C(18)-C(17)	117.7(8)
C(5)-C(6)-H(6)	118.9	O(6)-C(19)-C(20)	125.9(8)
C(7)-C(6)-H(6)	118.9	O(6)-C(19)-C(18)	113.2(8)
C(2)-C(7)-C(6)	119.4(9)	C(20)-C(19)-C(18)	120.9(8)
C(2)-C(7)-H(7)	120.3	C(19)-C(20)-C(15)	121.1(9)
C(7)-C(6)-H(6)	120.3	C(19)-C(20)-H(20)	119.5
C(9)-C(8)-C(5)	126.9(10)	C(15)-C(20)-H(20)	119.5
C(9)-C(8)-H(8)	116.5	O(6)-C(21)-H(21A)	109.5
C(5)-C(8)-H(8)	116.5	O(6)-C(21)-H(21B)	109.5
C(8)-C(9)-C(10)	123.6(9)	H(21A)-C(21)-H(21B)	109.5
C(8)-C(9)-H(9)	118.2	O(6)-C(21)-H(21C)	109.5
C(10)-C(9)-H(9)	118.2	H(21A)-C(21)-H(21C)	109.5
O(3)-C(10)-C(11)	125.9(9)	H(21B)-C(21)-H(21C)	109.5
O(3)-C(10)-C(9)	114.9(9)	C(3)-O(1)-C(1)	119.2(8)
C(11)-C(10)-C(9)	118.9(8)	C(3)-O(1)-Zn(1)	109.7(5)
C(10)-C(11)-C(12)	128.5(8)	C(1)-O(1)-Zn(1)	130.2(7)
C(10)-C(11)-H(11)	115.8	C(2)-O(2)-Zn(1)	118.6(5)
C(12)-C(11)-H(11)	115.8	C(2)-O(2)-Zn(2)	139.3(5)
O(4)-C(12)-C(11)	124.2(8)	Zn(1)-O(2)-Zn(2)	100.9(2)
O(4)-C(12)-C(13)	115.2(9)	C(10)-O(3)-Zn(2)#1	122.5(6)
C(11)-C(12)-C(13)	120.6(8)	C(12)-O(4)-Zn(2)#1	122.3(6)
C(14)-C(13)-C(12)	120.9(8)	C(18)-O(5)-Zn(2)#2	124.2(5)
C(14)-C(13)-H(13)	119.5	C(18)-O(5)-Zn(1)#3	124.3(5)
C(12)-C(13)-H(13)	119.5	Zn(2)#2-O(5)-Zn(1)#3	101.3(2)
C(13)-C(14)-C(15)	128.2(9)	C(19)-O(6)-C(21)	119.5(7)
C(13)-C(14)-H(14)	115.9	C(19)-O(6)-Zn(2)#2	109.5(5)
C(15)-C(14)-H(14)	115.9	C(21)-O(6)-Zn(2)#2	130.8(6)
C(16)-C(15)-C(20)	117.6(8)	O(2)-Zn(1)-O(2)#4	167.6(3)
C(16)-C(15)-C(14)	116.4(8)	O(2)-Zn(1)-O(5)#5	110.6(2)
C(20)-C(15)-C(14)	126.0(9)	O(2)#4-Zn(1)-O(5)#5	78.0(2)

O(2)-Zn(1)-O(5)#6	78.0(2)	O(1)-Zn(1)-Zn(2)#4	101.78(16)
O(2)#4-Zn(1)-O(5)#6	110.6(2)	O(4)#7-Zn(2)-O(3)#7	96.6(3)
O(5)#5-Zn(1)-O(5)#6	95.9(3)	O(4)#7-Zn(2)-O(5)#6	150.3(3)
O(2)-Zn(1)-O(1)#4	94.6(2)	O(3)#7-Zn(2)-O(5)#6	108.7(3)
O(2)#4-Zn(1)-O(1)#4	76.0(2)	O(4)#7-Zn(2)-O(2)	106.7(2)
O(5)#5-Zn(1)-O(1)#4	153.9(2)	O(3)#7-Zn(2)-O(2)	111.8(3)
O(5)#6-Zn(1)-O(1)#4	95.8(3)	O(5)#6-Zn(2)-O(2)	78.7(2)
O(2)-Zn(1)-O(1)	76.0(2)	O(4)#7-Zn(2)-O(6)#6	85.6(2)
O(2)#4-Zn(1)-Zn(1)	94.6(2)	O(3)#7-Zn(2)-O(6)#6	108.2(3)
O(5)#5-Zn(1)-O(1)	95.8(3)	O(5)#6-Zn(2)-O(6)#6	72.0(2)
O(5)#6-Zn(1)-O(1)	153.9(2)	O(2)-Zn(2)-O(6)#6	136.2(2)
O(1)#4-Zn(1)-O(1)	83.5(4)		
O(2)-Zn(1)-Zn(2)#4	149.17(18)		
O(2)#4-Zn(1)-Zn(2)#4	40.04(17)		
O(5)#5-Zn(1)-Zn(2)#4	38.56(15)		
O(5)#6-Zn(1)-Zn(2)#4	101.91(16)		
O(1)#4-Zn(1)-Zn(2)#4	115.91(15)		

Symmetry transformations used to generate equivalent atoms:

#1 -x+1,-x+y+1,-z+5/3 #2 y+1,x+1,-z+2

#3 x+1,y+1,z #4 y,x,-z+2 #5 x-1,y-1,z

#6 y-1,x-1,-z+2 #7 -x+1,-x+y,-z+5/3

Table S4. Anisotropic displacement parameters ($Å^2 \times 10^3$)for medi-MOF-1. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U^{11} + ... + 2 h k a^* b^* U^{12}]$.

	U11	U22	U33	U23	U13	U12
C(1)	280(20)	74(10)	61(8)	1(7)	47(11)	39(12)
C(2)	47(6)	45(6)	44(5)	-1(4)	-5(4)	10(5)
C(3)	64(7)	46(6)	42(5)	0(4)	8(5)	15(5)
C(4)	79(8)	41(6)	56(6)	-2(5)	7(6)	3(6)
C(5)	93(9)	45(6)	61(6)	14(5)	0(7)	9(7)
C(6)	137(12)	57(7)	36(5)	2(5)	5(7)	15(8)
C(7)	89(9)	60(7)	40(5)	-3(5)	9(6)	17(7)
C(8)	89(9)	53(7)	52(6)	6(5)	-8(6)	-6(7)
C(9)	85(9)	75(8)	41(6)	21(6)	2(6)	10(7)
C(10)	51(6)	46(6)	39(5)	12(4)	2(4)	10(5)
C(11)	66(7)	53(6)	39(5)	12(5)	1(5)	6(6)
C(12)	59(6)	58(7)	43(5)	-2(5)	-13(5)	29(6)
C(13)	77(8)	60(7)	34(5)	3(5)	-7(5)	29(6)
C(14)	45(6)	63(7)	59(6)	-1(5)	-12(5)	16(6)
C(15)	46(6)	59(7)	40(5)	3(5)	-3(4)	17(5)
C(16)	47(6)	78(8)	43(5)	2(5)	-12(5)	15(6)
C(17)	52(7)	74(8)	49(6)	21(5)	12(5)	16(6)
C(18)	46(6)	50(6)	39(5)	-5(5)	2(4)	17(5)
C(19)	57(6)	52(6)	35(5)	1(4)	3(4)	20(5)
C(20)	41(6)	49(6)	56(6)	5(5)	-1(5)	4(5)
C(21)	77(8)	82(9)	69(7)	26(7)	-7(6)	20(7)
O(1)	112(6)	39(4)	40(4)	1(3)	22(4)	16(4)
O(2)	52(4)	37(4)	43(3)	0(3)	5(3)	9(3)
O(3)	60(4)	43(4)	46(4)	14(3)	-3(3)	-3(3)
O(4)	50(4)	50(4)	37(3)	5(3)	-4(3)	17(3)
O(5)	39(4)	57(4)	39(3)	-13(3)	-5(3)	17(3)
O(6)	52(4)	66(5)	43(4)	9(3)	-5(3)	13(4)
Zn(1)	45(1)	45(1)	36(1)	-3(1)	3(1)	10(1)
Zn(2)	44(1)	51(1)	37(1)	-8(1)	-1(1)	23(1)

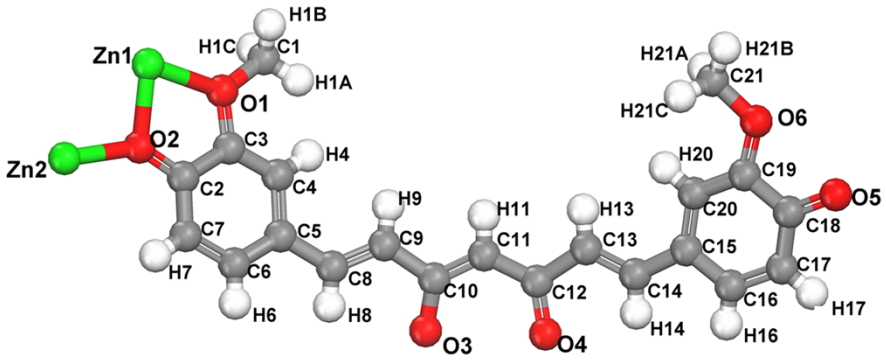

Fig. S2 The asymmetric unit present in crystal structure with all atoms.

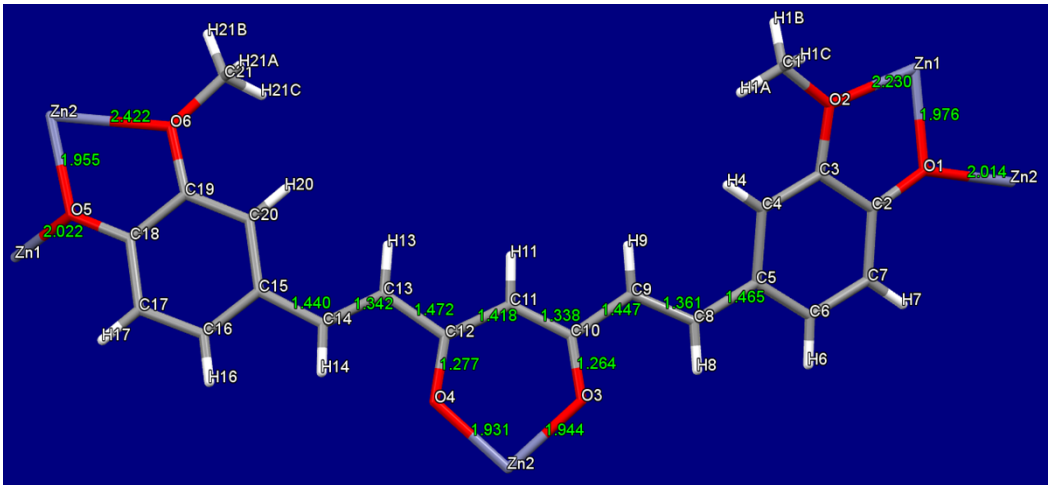

Fig. S3 The bond lengths in medi-MOF-1.

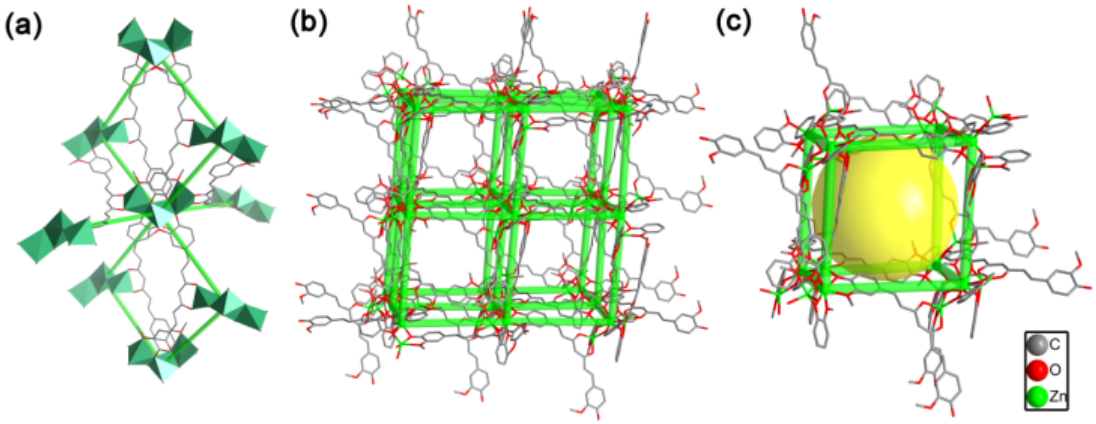

Fig. S4 (a) Topology analysis of medi-MOF-1 (Polyhedra: Zn clus-ters); (b) pcu lattice; (c) one pcu lattice cell with yellow ball in the pore.

3. Ibuprofen controlled release experiments

Incorporation of ibuprofen: A typical procedure for loading ibuprofen in medi-MOF-1 was described as follows: ibuprofen was entrapped into the porous solids by suspending the 200 mg of the desolvated powder material in 10 mL of 0.1 M ibuprofen hexane solution under stirring for 12 h while preventing the evaporation of hexane. The ibuprofen-containing solids were recovered by filtration, washed with hexane to remove the extra ibuprofen, and dried at 100 °C to remove the remaining hexane. Filtrate was collected, then sucked and diluted properly to calculate the ibuprofen-loading amount into the porous solids by UV-Vis spectrophotometer. The structures of medi-MOF-1 are retained after drug adsorption, which can be proved by PXRD measurement.

Calibration plot of standard Ibuprofen: Seven Ibuprofen solutions with concentrations of 1, 2, 4, 10, 20, 40 and 50 μg/mL in PBS were prepared as standards. The calibrated plot exhibited a good correlation coefficient 0.9997 (Figure S4). The content of released ibuprofen was calculated as follows:

$$A = 0.0137 + 0.0428\ C$$

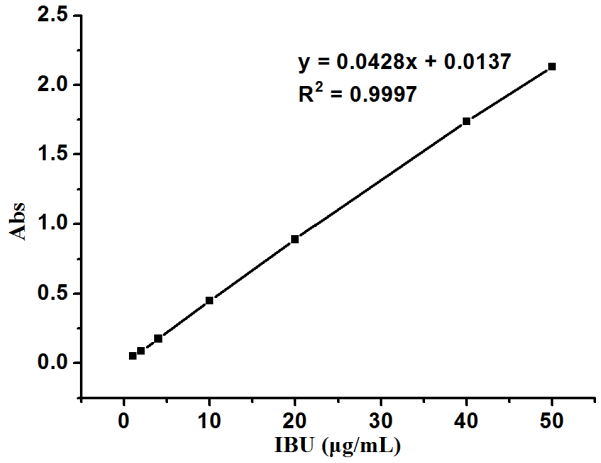

Fig. S5 Calibration plot of standard Ibuprofen in PBS obtained by UV-Vis spectrophotometer at 222 nm.

Ibuprofen release Experiment: 10 mg of the drug-loaded samples were dispersed in 5 mL of simulated body fluid (PBS, pH = 7.4, buffer solution) and sealed in a dialysis bag (molecular weight cutoff = 8000). After the dialysis bag submerged in 55 mL

respective solutions and stirred at 37 °C for 80 h, 3 mL samples were collected at predetermined time intervals (half hr in 2 hrs, one hr in the next 8 hrs, 6 hr (day) or 12 hr (night) in the rest time) and analyzed the content of released ibuprofen by UV/Vis spectroscopy at 222 nm wavelength. Then the fresh PBS buffer solution was added to the system in order to keep the volume constant.

4. In vitro degradation of medi-MOF-1

The degradation of medi-MOF-1 crystals were investigated by suspending 2 mg of activated medi-MOF-1 and the drug-loaded samples in 5 mL of PBS (pH 7.4) at 37 °C. At first, all the same suspension of medi-MOF-1 in PBS were prepared. These solutions were kept stirring for predetermined time intervals. At each time point, one of these suspensions was recovered by centrifugation (10000 rpm, 3 min) and washed with water for 3 times. Then the solid was dissolved in 5 mL absolute ethanol in order to detect the concentration of curcumin which was degraded from the material. The concentration of released organic linker curcumin was quantified by UV-Vis spectrophotometer with the supernatant at 425 nm wavelength. The content of degraded curcumin was calculated as follows:

$$A = 0.015 + 0.1396\ C$$

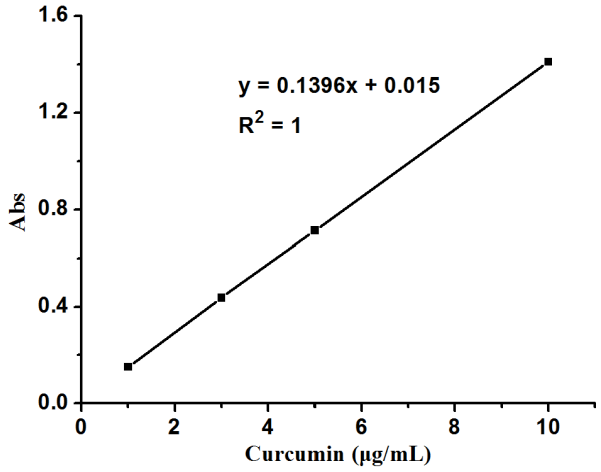

Fig. S6 Calibration plot of standard Curcumin in absolute ethanol obtained by UV-Vis spectrophotometer at 425 nm**.**

5. In vitro cytotoxicity assay

Cell Culture: The cytotoxicity of cells in the presence of medi-MOF-1 was studied by MTT (3-[4,5-dimethylthialzol-2-yl]-2,5-diphenyltetrazolium bromide, Sigma) assay. For MTT assay, pancreatic cancer cells (BxPC-3) were incubated in monolayer in Dulbecco's Modified Eagle's Medium (DMEM, Gibco) supplemented with 5% (v/v) fetal bovine serum (FBS, Gibco) and penicillin/streptomycin (100 U/mL and 100 μg/mL, respectively, Gibco) under an atmosphere of 5% CO_2 at 37°C.

Cell Viability: BxPC-3 cells were seeded into 96-well plates at a density of 8×10^3 per well in 100 μL of media and grown overnight. Afterward, medi-MOF-1(after grinding), corresponding concentration of $Zn(OAc)_2 \cdot 2H_2O$ and curcumin were respectively added into the cells, with various concentrations from 0 to 50 μg/mL for 72h. Following this incubation, 10 μL per well of MTT solution (5 mg/mL phosphate buffered saline) was added for another 4 h. The precipitated formazan violet crystals were dissolved in 100 μL of 10 % SDS in 10 mmol HCl solution at 37°C overnight. The colour intensity of the formazan solution, which reflects the cell growth condition, was measured at 570nm by multi-detection microplate reader (SynergyTM HT, BioTek Instruments Inc, USA).

6. Thermogravimetric analysis

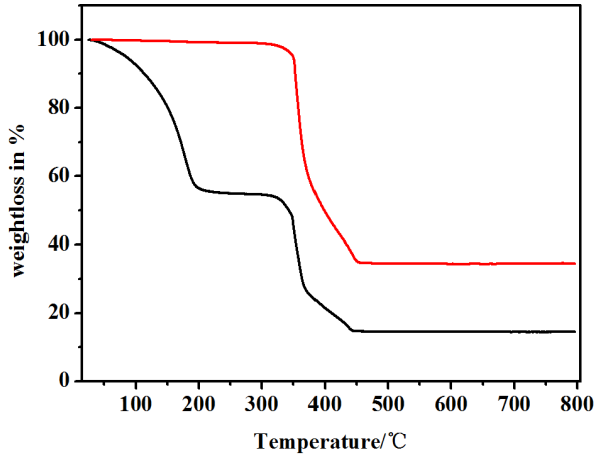

Fig. S7 Thermogravimetric analysis of medi-MOF-1: as-synthesized (black) and ctived by CH_2Cl_2 (red).

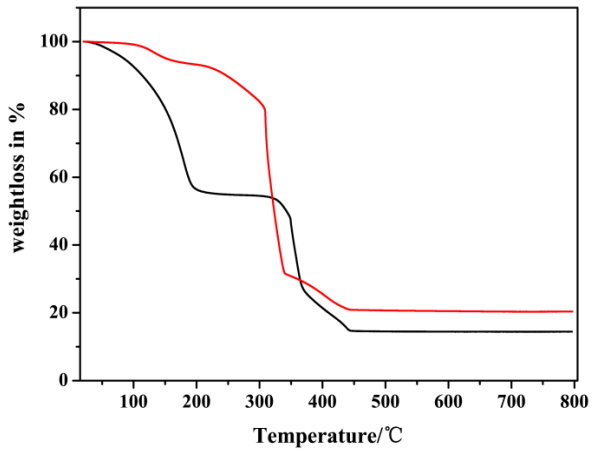

Fig. S8 Thermogravimetric analysis of as-synthesized (black) and drug-loaded (red) medi-MOF-1 under air atmosphere.

The TGA data reveals a continuous weight loss of 45.2% from room temperature to 200 °C, which can be attributed to the loss of guest molecules (calc. 44.66%). The following is a plateau in the range of 200-350 °C which indicates the stability of the empty porous framework. The decomposition of medi-MOF-1 occurs between 350 and 450 °C with a weight loss of 40.35% (calcd. 40.76%), and the residue from 450-800 °C corresponds to the remained ZnO (calcd. 14.99%, obs. 14.56%).

7. Powder X-ray diffraction patterns

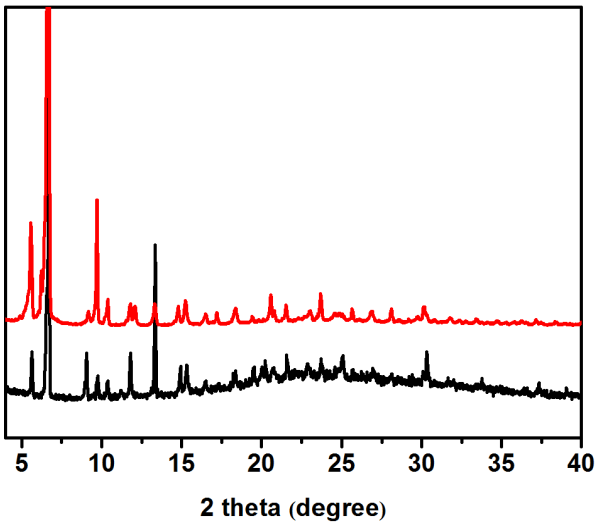

Fig. S9 PXRD patterns of medi-MOF-1: as synthesized (black); activated by CH_2Cl_2 (red).

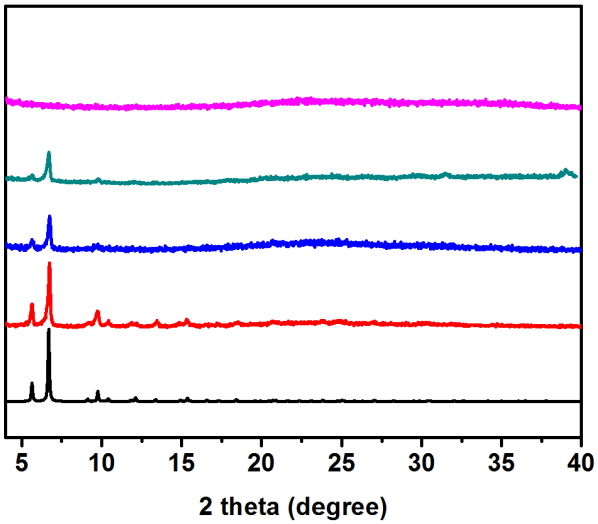

Fig. S10 PXRD patterns of medi-MOF-1 after calcination in air: as synthesized (black); 200°C (red); 250°C (blue); 300°C (green); 350°C (pink).

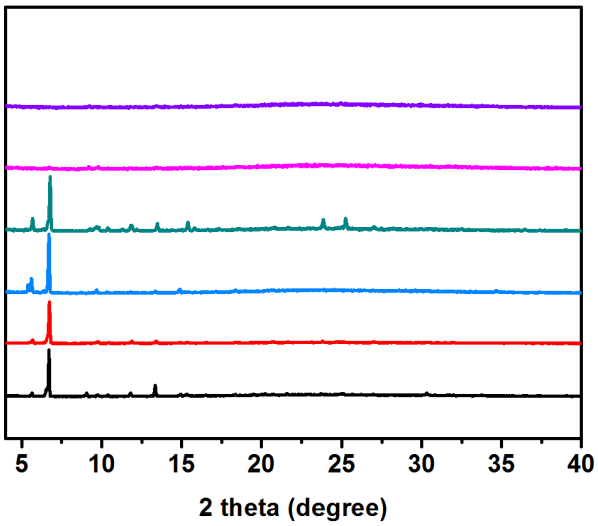

Fig. S11 PXRD patterns of medi-MOF-1: as synthesized (black); in absolute ethanol (red); in CH_2Cl_2 (blue); in n-hexane (green); in PBS (pink); in water (purple).

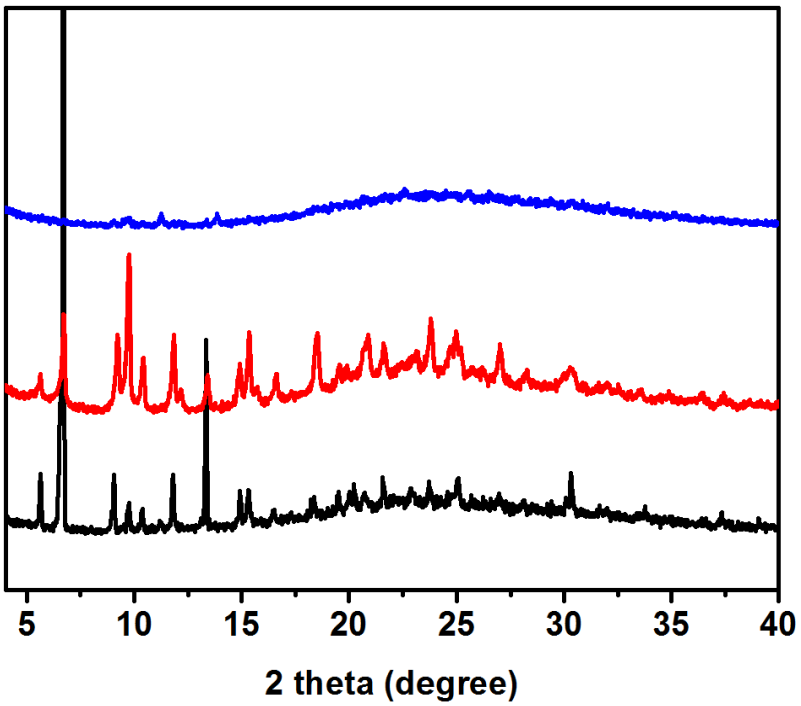

Fig. S12 XRD patterns of medi-MOF-1: as synthesized (black); ibuprofen-loaded (red); after drug release experiments (blue).

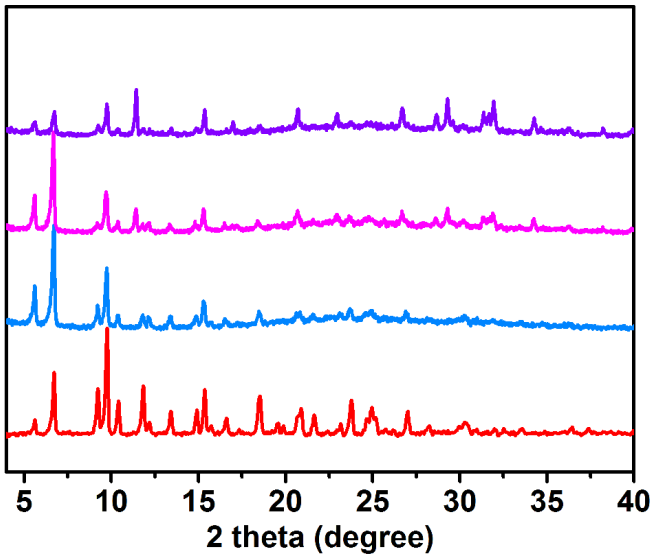

Fig. S13 XRD patterns of activated medi-MOF-1 (red); after immersing in PBS for 1h (blue); 4h (pink); and 12h (purple).

8. IR spectrum

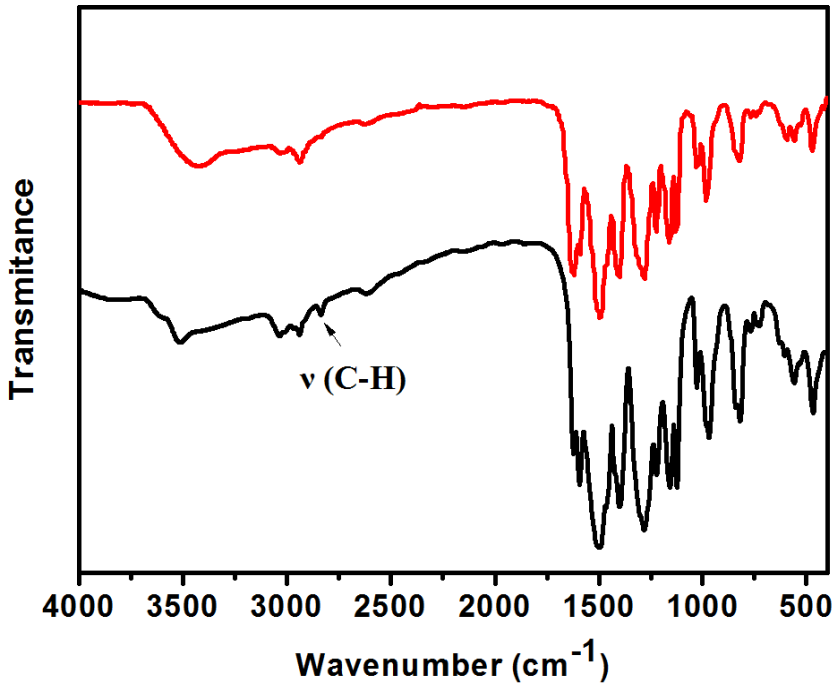

Fig. S14 FTIR spectra of medi-MOF-1: as-synthesized (black); activated by CH_2Cl_2 (red).

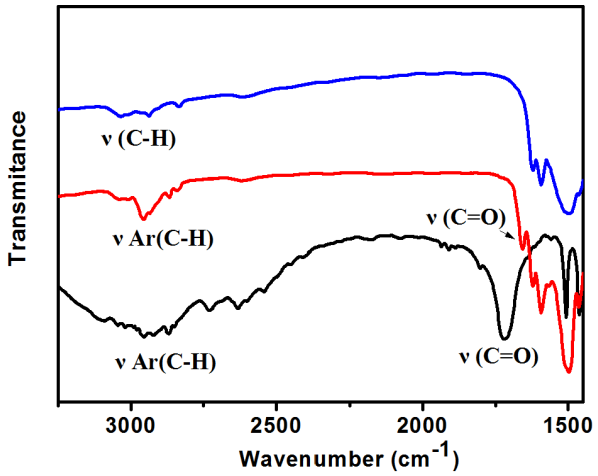

Fig. S15 FTIR spectra: ibuprofen (black); ibuprofen-loaded medi-MOF-1 (red); as-synthesized medi-MOF-1 (blue).

In the FTIR spectra of the Ibuprofen-containing samples can be observed the ν Ar(C-H) bands around 2956cm^{-1} and 2870cm^{-1}, corresponding to the C-H groups from the aromatic groups. Besides, the shift of the ν(C=O) band from 1725 cm^{-1} to 1656 cm^{-1} in the Ibuprofen-containing samples, revealed the presence of ibuprofen carboxylic group.

9. Pore size distribution of medi-MOF-1

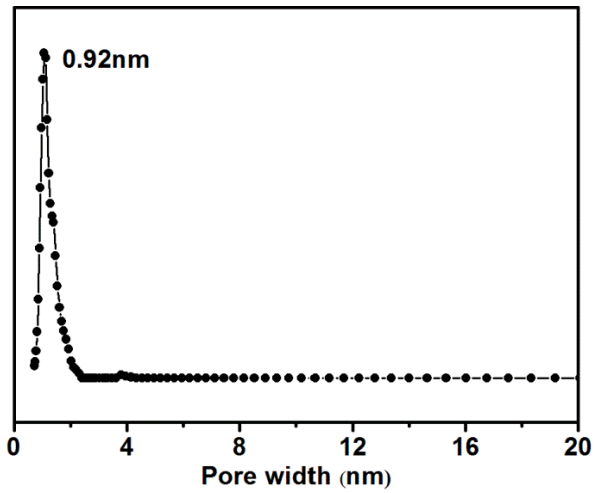

Fig. S16 Pore size distribution calculated by NLDFT model.

10. Images of medi-MOF-1

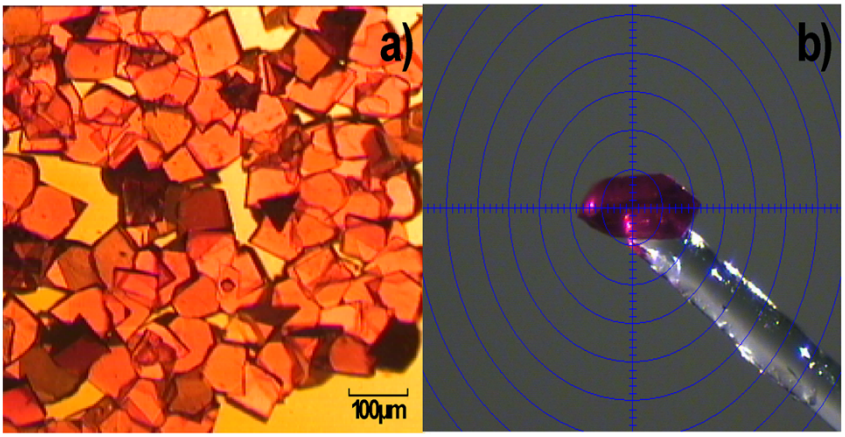

Figure S17 (a) Light microscope image of solvated bulk medi-MOF-1 crystals (scale bar = 100 μm); (b) image of single crystal X-ray different measurement (20 μm for one scale).

11. In vitro co-delivery of medi-MOF-1

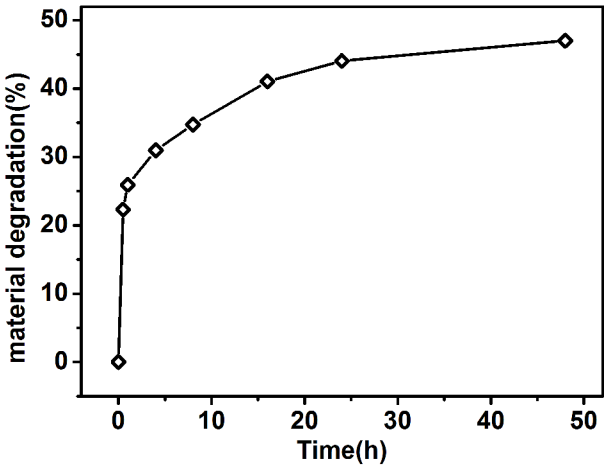

Fig. S18 The curcumin release of ibuprofen-loaded medi-MOF-1 sample