

Supporting Information

Multivariate Metal-Organic Frameworks based pH-responsive dual-drug delivery system for chemotherapy and chemodynamic therapy

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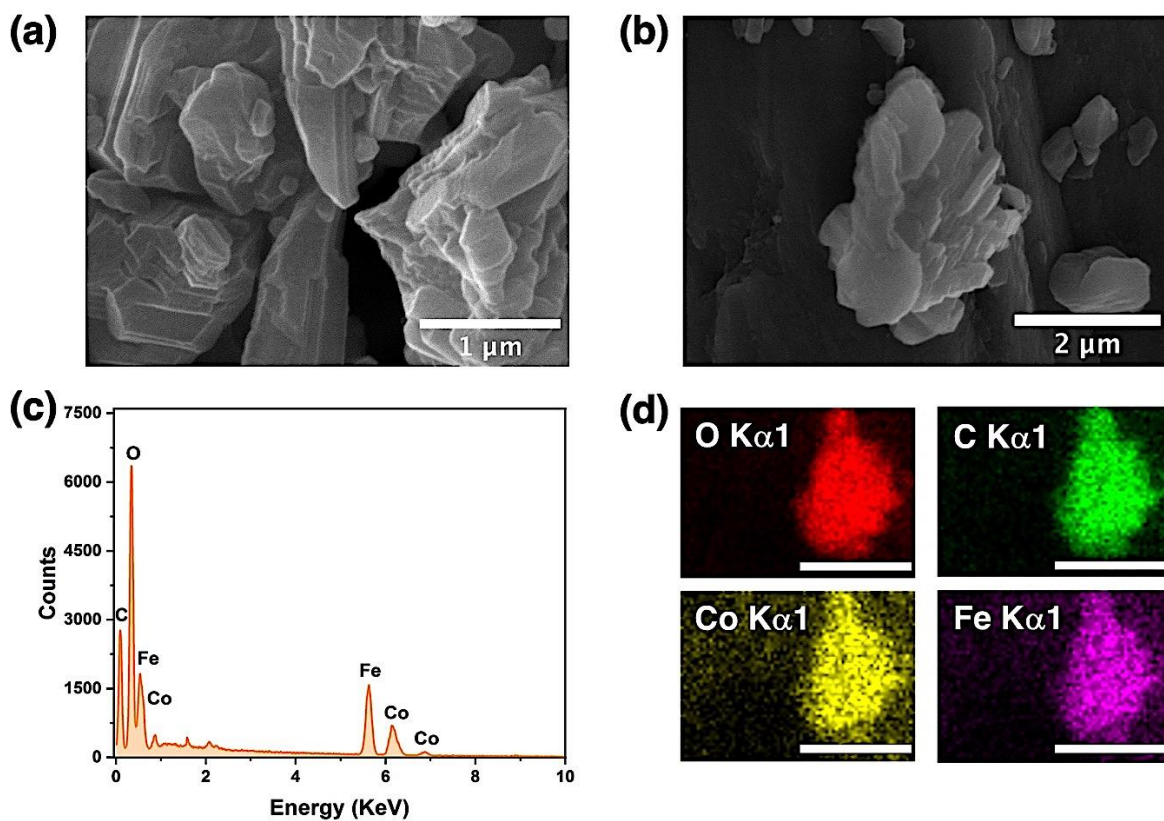


Figure S1. SEM images (a-b), EDX spectra (b), and elemental map (c) of FeCo-cluster

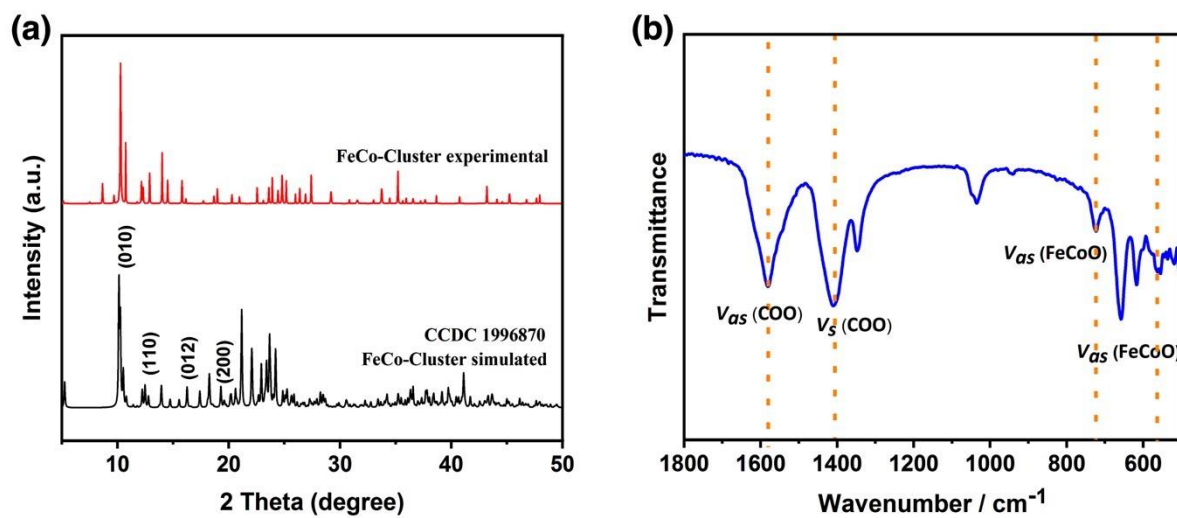


Figure S2. PXRD pattern (a), and FT-IR spectra (b) of FeCo-cluster

Table S1. The metal composition of FeCo-cluster and MTV-1 MOFs obtained by EDX and ICP-OES

Sample	OES	
	EDX n(Fe) : n(Co)	ICP-OES n(Fe) : n(Co)
FeCo-Cluster	2.02 : 1	1.88 : 1
MTV-1	1.94 : 1	1.83 : 1

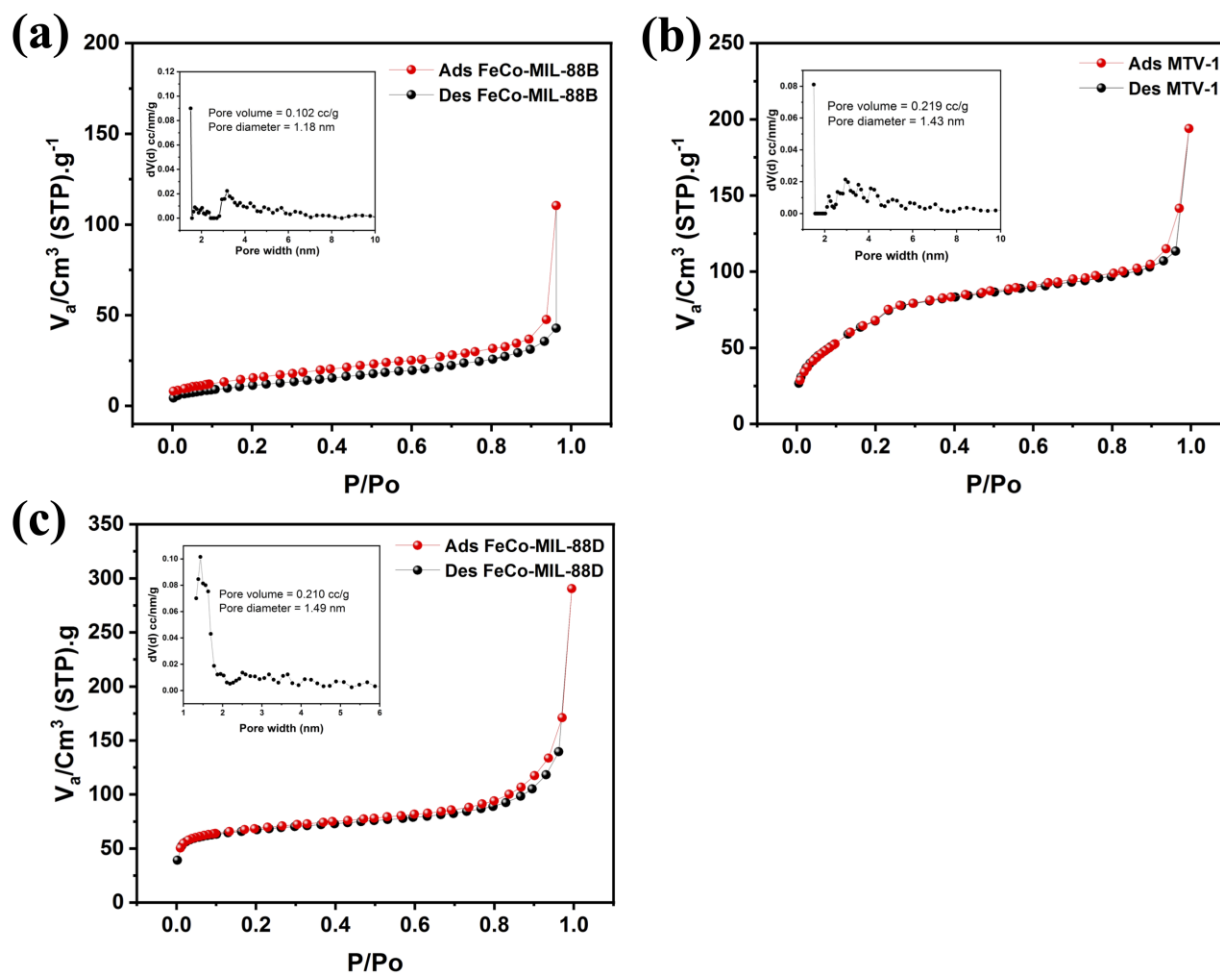


Figure S3. N_2 adsorption-desorption isotherm of FeCo-MIL-88B (a), MTV-1 (b), and FeCo-MIL-88D (c) with insets = pore dynamics.

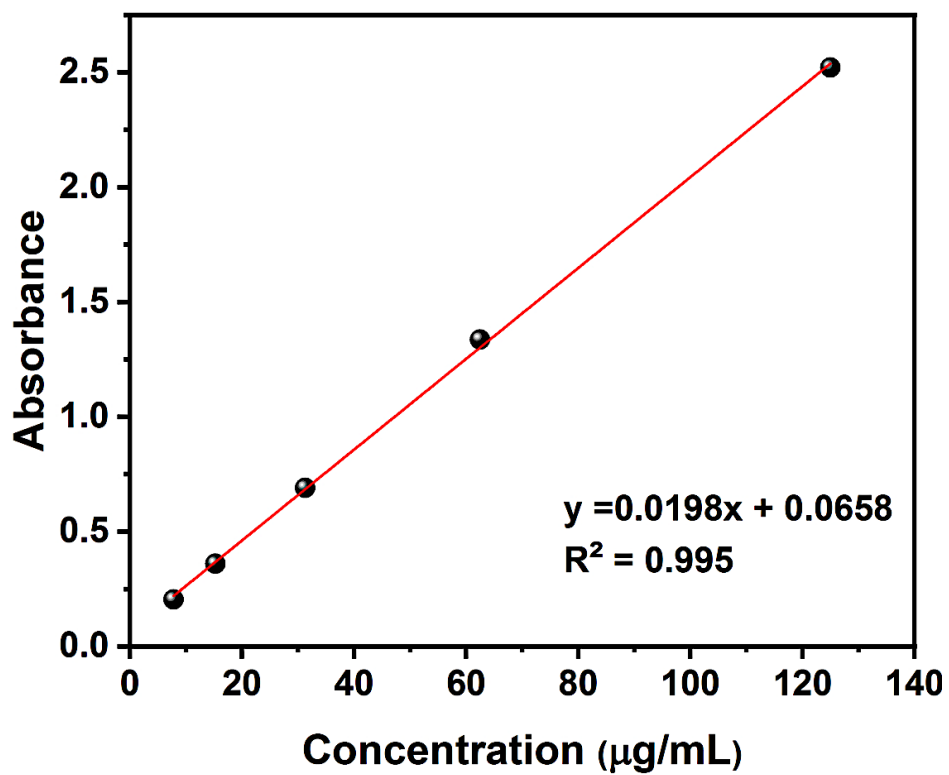


Figure S4. Calibration curve of 5-FU in ethanol

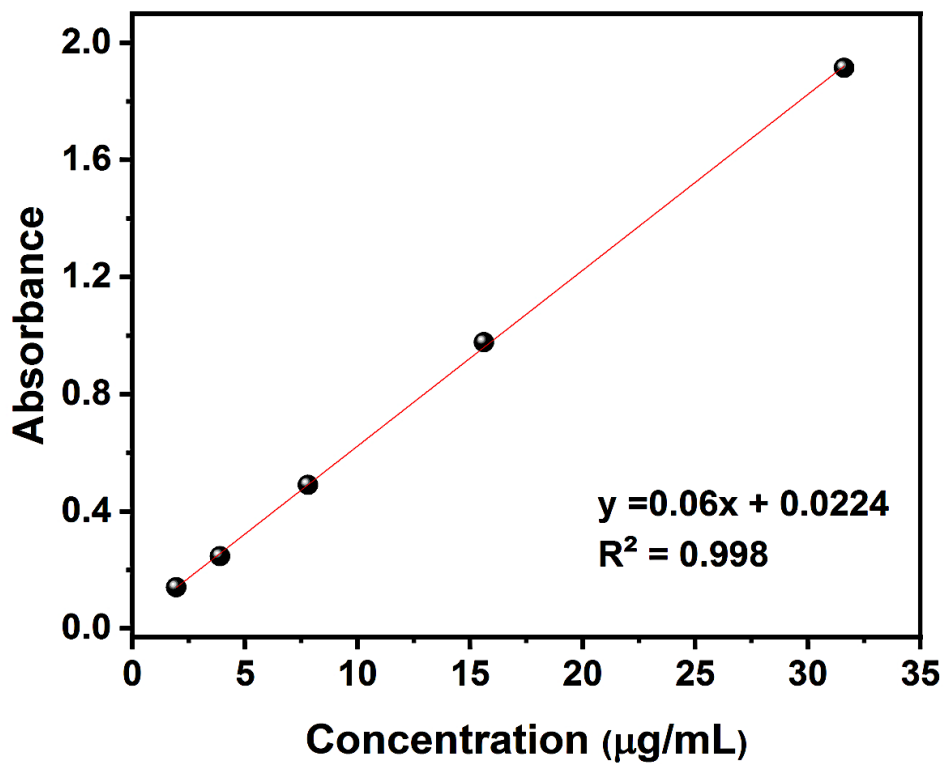


Figure S5. Calibration curve of CUR in ethanol

Table S2. Drug loading capacity of different MOFs for 5-FU and CUR

Type of MOF	5-FU loading (wt%)	CUR loading (wt%)
FeCo-MIL-88B	22.6	0.5
FeCo-MIL-88D	19.7	3.5
MTV-1	15.1	9.3

Table S3. The IR peaks of 5-Fluorouracil and Curcumin spectrum

Wavenumber (cm ⁻¹)	Functional groups
5-FU	
740	CF = CH group vibrations
800	C-F wagging band
1240	C-N vibrational band
1710	C = O carbonyl stretching
CUR	
974	C = C benzene ring stretching
1278	C-O aromatic stretching
1594	C-O-C stretching
3200-3500	stretching band in enol form

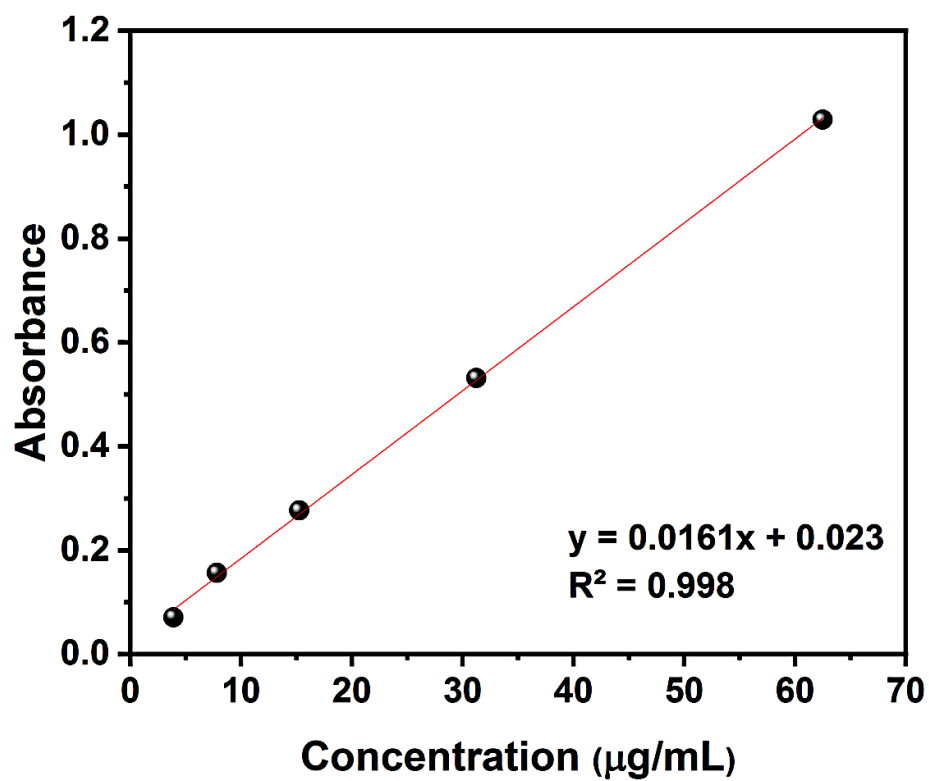


Figure S6. Calibration curve of 5-FU in PBS

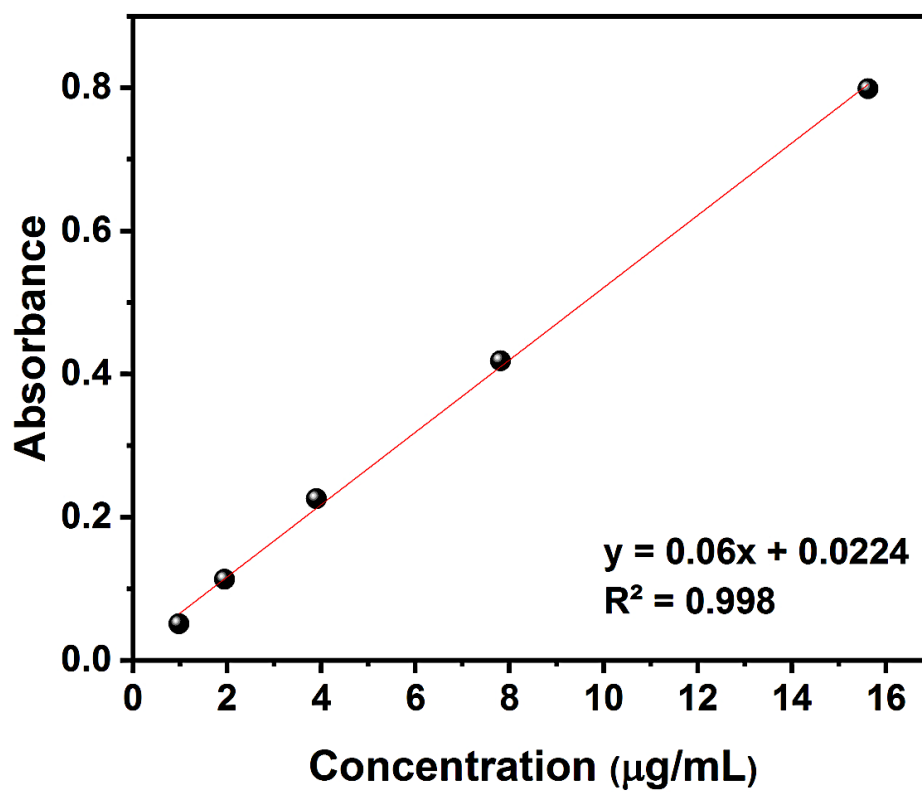


Figure S7. Calibration curve of CUR in PBS

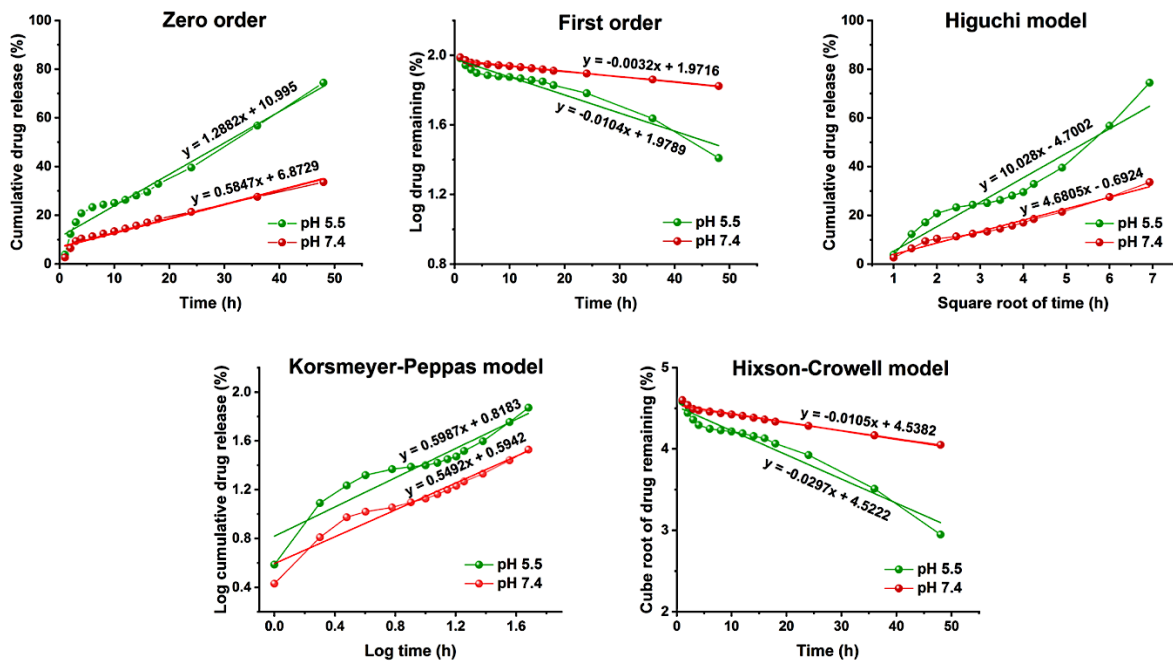


Figure S8. Application of 5-FU release data on mathematical release models for MTV-1@5-FU+CUR at pH = 5.5 and 7.4

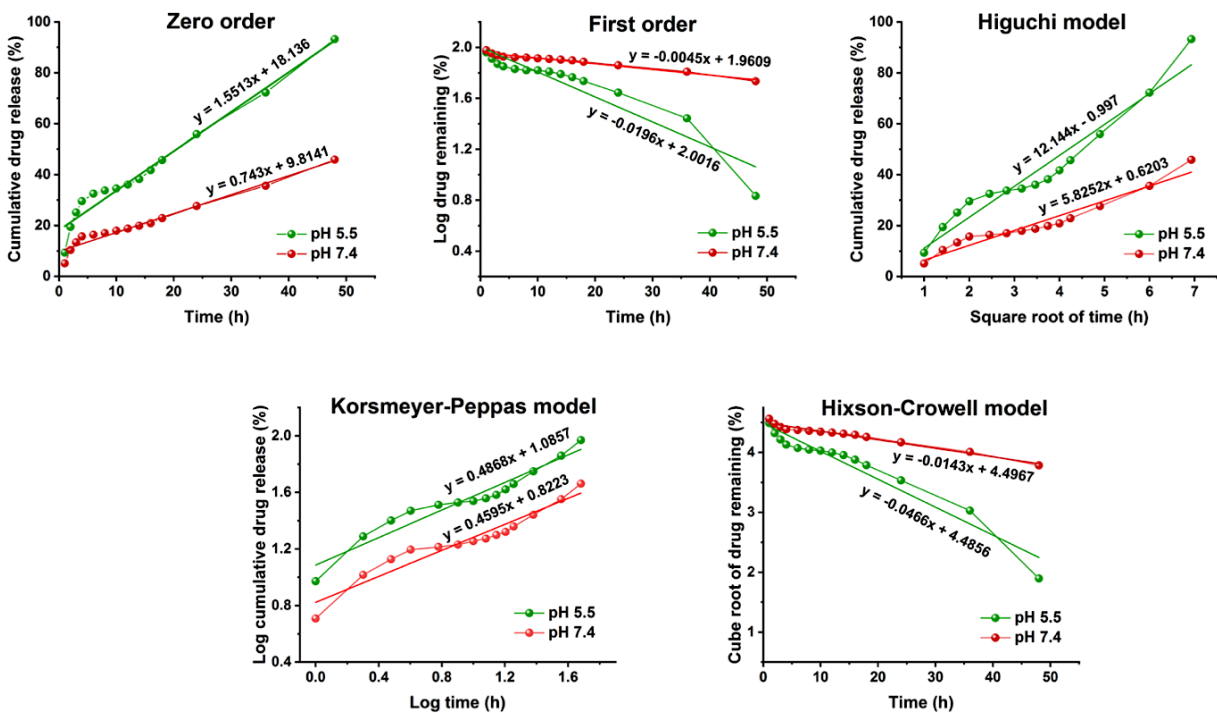


Figure S9. Application of CUR release data on mathematical release models for MTV-1@5-FU+CUR at pH = 5.5 and 7.4

Table S4. Kinetic release models with their mathematical formulas

Kinetic model	Formula
Zero order	$M_0 - M_t = K_0 t$
First order	$M_t = M_0 \cdot \exp^{-k_1 t}$
Higuchi	$M_t = k_t^{1/2}$
Korsmeyer-Peppas	$M_t/M_\infty = k_{KP} \cdot t^n$
Hixson-Crowell	$1 - [1 - M_t/M_\infty]^{1/3} = 1 - K_{HC} \cdot t$

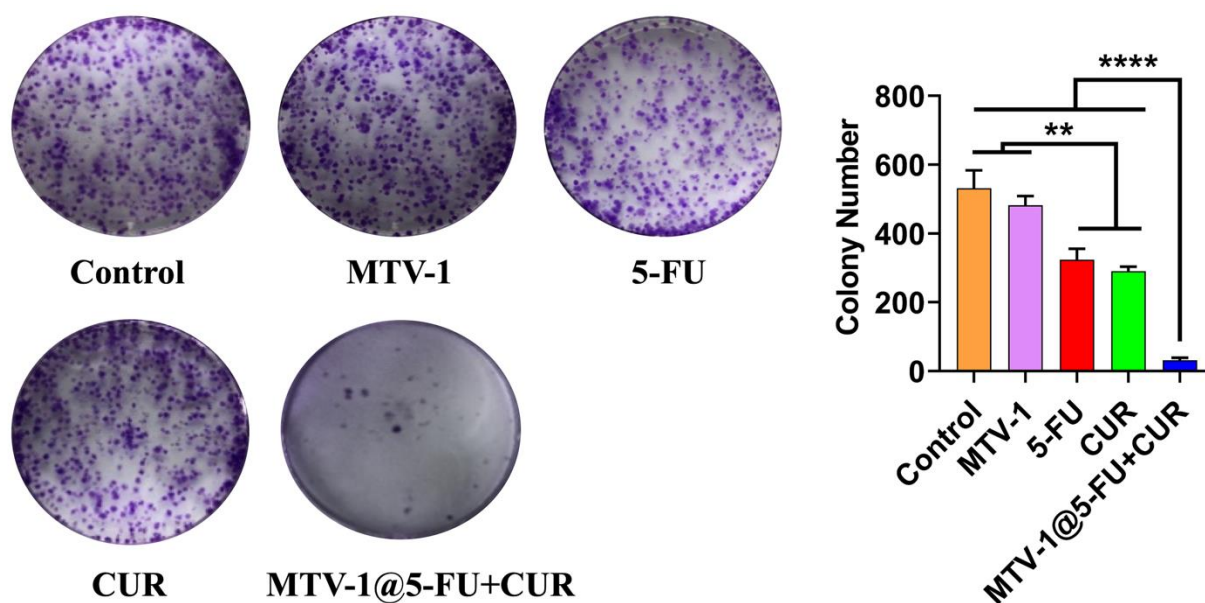


Figure S10. Colony formation assay results of HepG2 cells treated with 5-FU, CUR, MTV-1 and MTV-1@5-FU+CUR. Data are means \pm SD. (n=3); **P \leq 0.01 and ****P \leq 0.0001 compared with control.

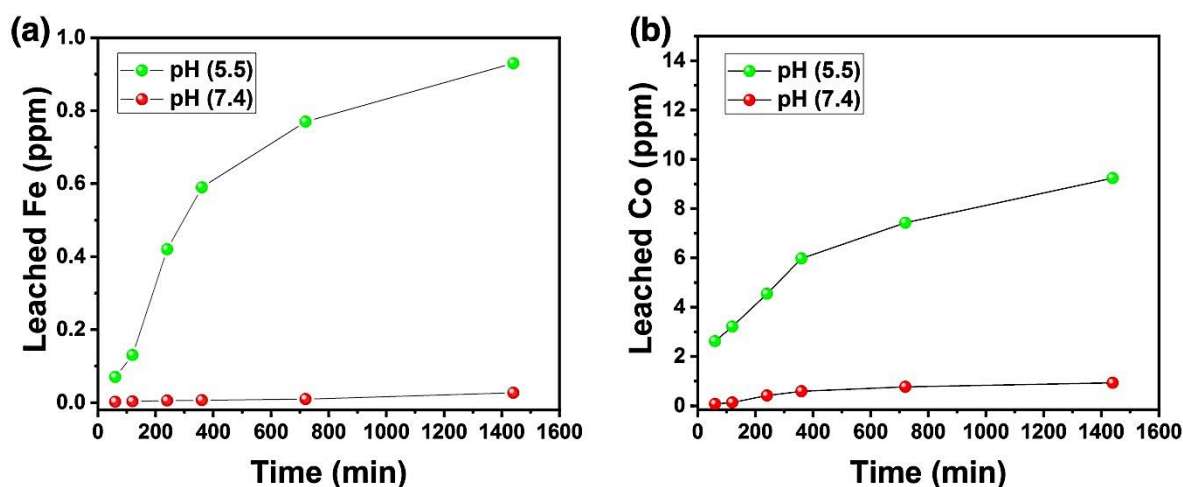


Figure S11. Fe ion release (a), and Co ion release (b) from MTV-1 in PBS (pH = 5.5 and 7.4)

Table S5. List of reported MOFs for multi-drug delivery.

MOFs	Loaded Drugs	Stimuli	Cell lines	Therapy	References
UiO-67	5-FU + PMT	pH	A549, HeLa Cells	CT	1
ZIF-8	DOX + CPT	pH NIR laser	HepG2 cells	CT and PTT	2
ZIF-90	DOX + 5-FU	pH	-	-	3
ZIF-8	DOX + VER	pH	MCF-7	CT	4
Mixed ligand MOFs	IBU + DOX	pH	HEK-293A	-	5
MTV MOFs	DOX + IBU + RhB	Linker interaction	-	-	6
Zr-MOFs	5-FU + DCA	-	MCF-7	CT	7
ZIF-8	DOX + HCPT	pH	HepG2, HeLa and MCF-7 cells	CT and PTT	8
MIL-88B-on- UiO-66	5-FU + AL	-	MCF-7	CT	9
MOF-74	IBU + CUR	-	-	-	10
Core-Shell MOFs	DOX + CUR	pH	MCF-7 and HepG2	CT	11
Al-MOF/GO	5-FU + DOX	pH	MCF-7 and MCF- 10a	CT	12

MTV MOFs	5-FU + CUR	pH	HEK-293 and HepG2	CT and CDT	This work
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ABBREVIATIONS

CDT	Chemodynamic therapy
CT	Chemotherapy
CUR	Curcumin
DOX	Doxorubicin
GO	Graphene Oxide
HCPT	10-Hydroxycamptothecin
HEK-293	Human Embryonic Kidney cells
HepG2	Human Hepatocellular cancer cells
IBU	Ibuprofen
MCF	Michigan Cancer Foundation
MTV	Multivariate
NIR	Near Infrared
PMT	Pemetrexed
PTT	Photothermal Therapy
RhB	Rhodamine B
UiO	University of Oslo
VER	Verapamil
ZIF	Zeolite Imidazolate Framework

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