Supporting Information

Isosteric Substitution of *4H*-1,2,4-Triazole by *1H*-1,2,3-Triazole in Isophthalic Derivative for Tuning Self-Assembly of Soft Supramolecular Materials

Table of Contents

1. Click-TIA hydrogels

1.1. Devices for T_d determination

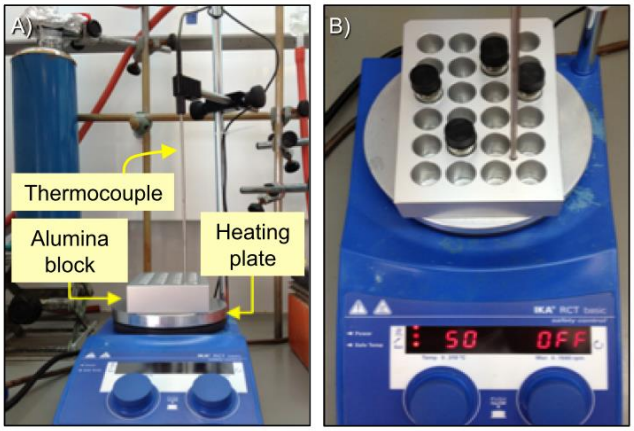
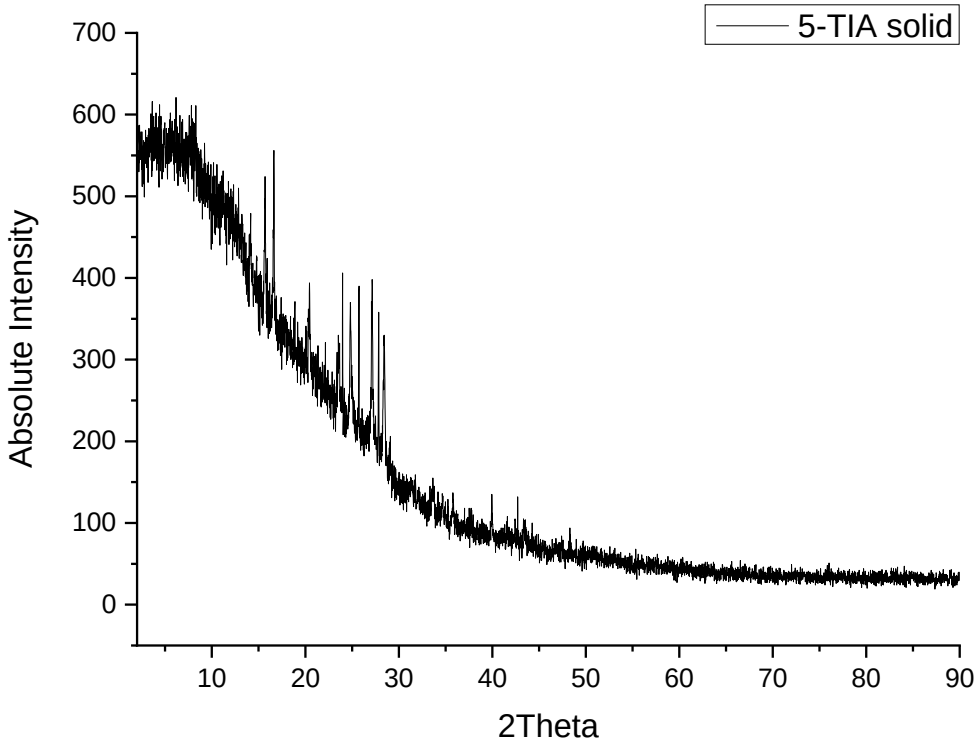


Figure S1. Custom-made set-up for T_d determinations. A) Front view of the set-up. B) Top view of the set-up during a typical experiment. The vials must fit smoothly inside the molds to ensure the optimal transmission of the heat flow.

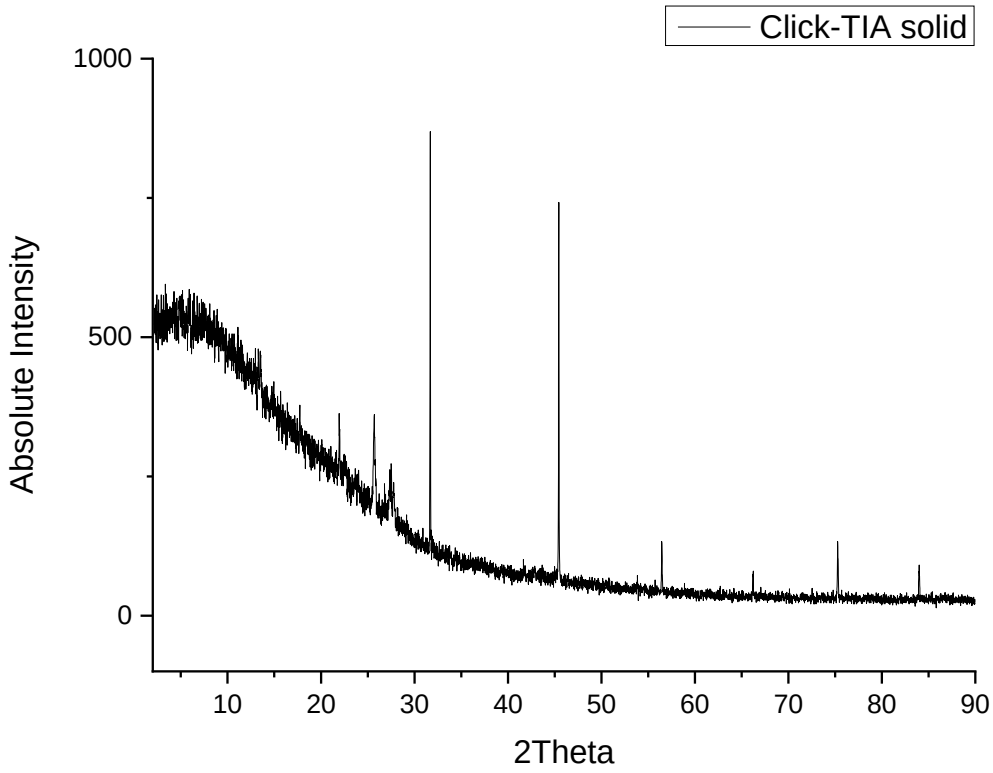
1.2. PXRD

a)



5-TIA solid	
2θ (°)	d (nm)
15.695	0.07700162
16.64	0.08619103
20.45	-0.10731546
23.54	-0.10771901
23.99	-0.14238548
24.815	-0.48671599
25.745	0.25549968
27.155	0.09086275
27.845	0.07880887
28.415	0.07719084
39.95	0.08532244
42.71	0.12960742

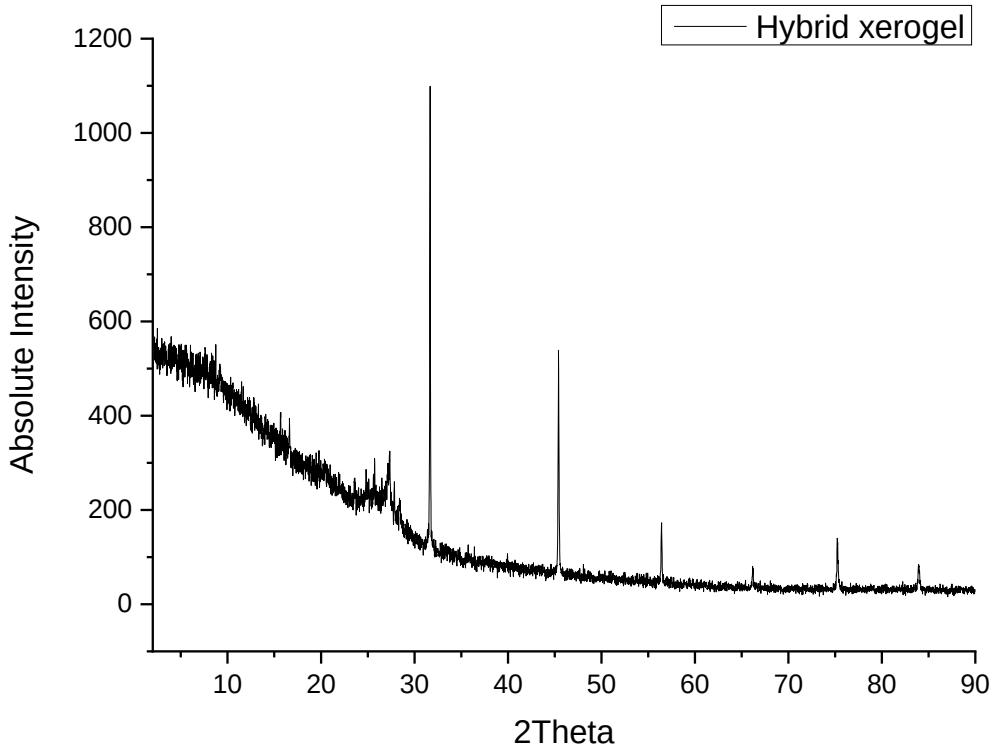
b)



Click-TIA solid

2θ (°)	d (nm)
21.95	-0.0770163
25.7	0.2751554
27.53	0.08265868
31.685	-0.57406461
45.44	-0.11561331
56.45	1.56142674
66.245	0.07771526
75.275	-1.25055076
83.99	-0.08419808

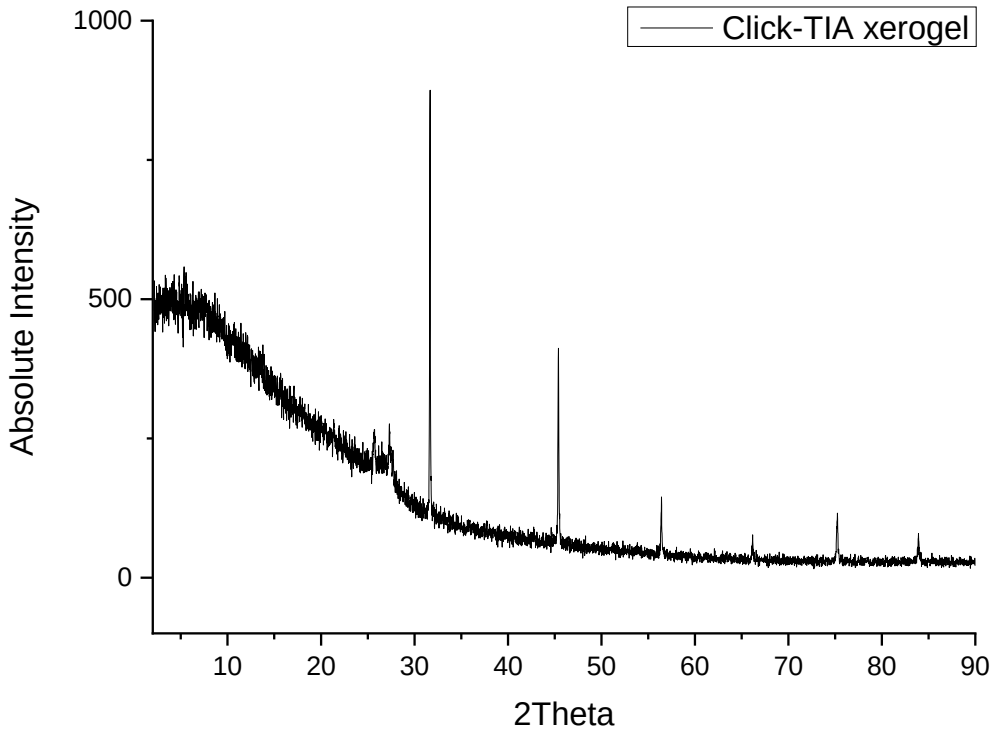
c)



Hybrid xerogel

2θ (°)	d (nm)
31.67	-0.60775728
45.41	-0.11760219
56.435	1.35555527
66.17	0.07737335
75.23	-0.91652811
83.945	-0.08506625

d)



Click-TIA xerogel

2θ (°)	d (nm)
31.67	-0.60775728
45.395	-0.11863264
56.42	1.197707
66.17	0.07737335
75.245	-1.0060504
83.915	-0.08567935

e)

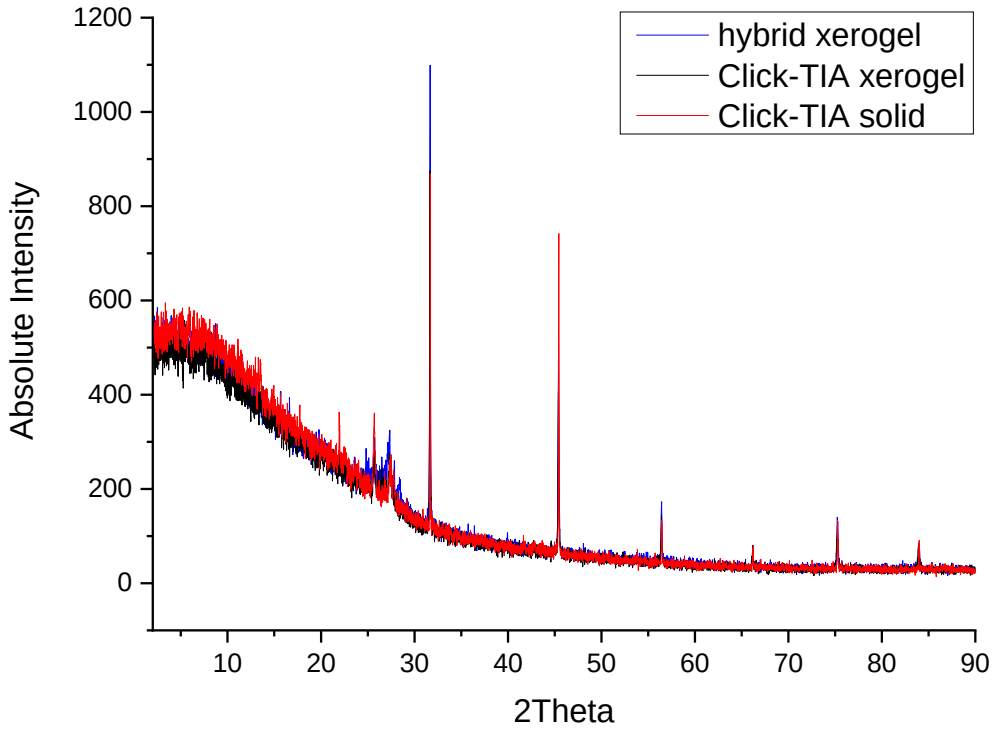


Figure S2. PXRD patterns and lattice spacings of a) **5-TIA** powder, b) **click-TIA** powder, c) hybrid xerogel prepared by freeze-drying the corresponding hybrid hydrogel derived from **click-TIA** and **5-TIA** (1:0.2), and d) **click-TIA** xerogel prepared by freeze-drying the hydrogel derived from **click-TIA**; e) Overlap spectra of b), c) and d).

1.3. Additional FE-SEM images

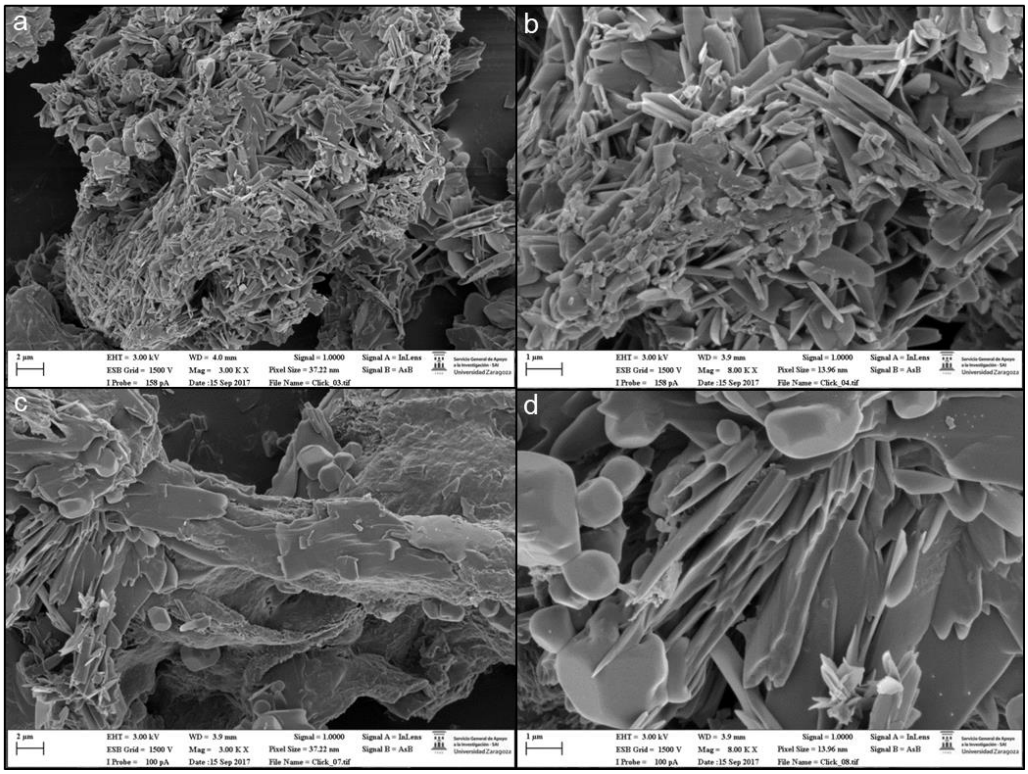


Figure S3. FE-SEM images of xerogels prepared by freeze-drying the hydrogel derived from **click-TIA** (c = 19 g L^{-1}).

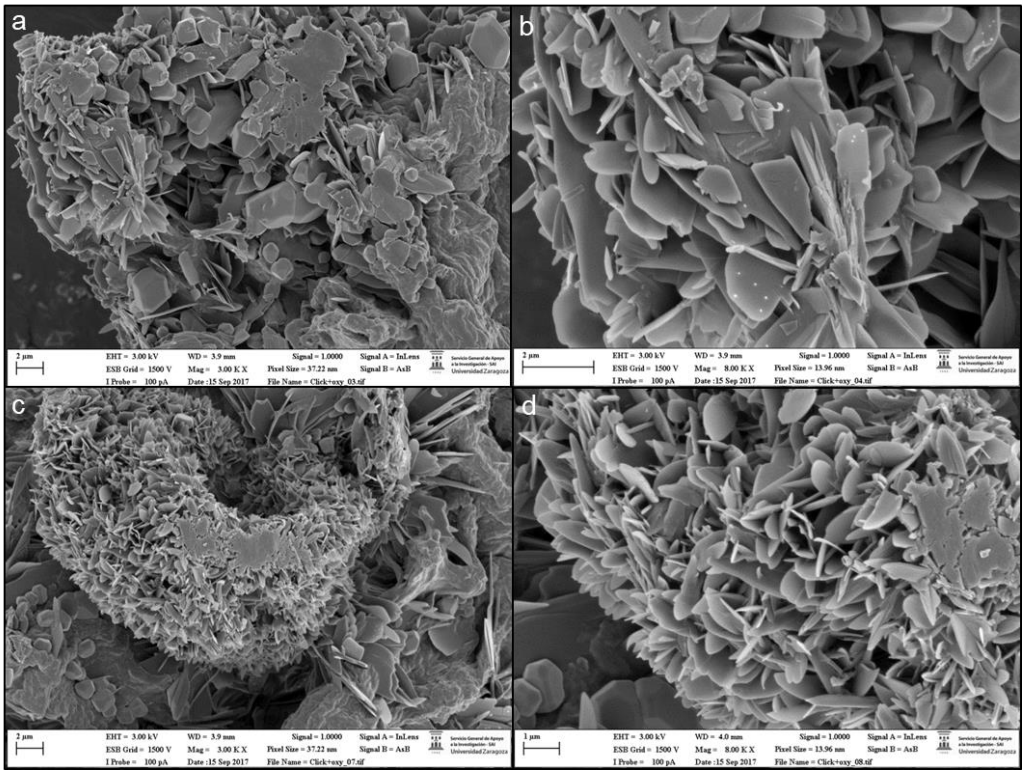


Figure S4. FE-SEM images of xerogels prepared by freeze-drying of the drug-loaded hydrogel derived from **click-TIA** (c = 19 g L^{-1}) and oxytetracycline hydrochloride (c = 0.8 g L^{-1}).

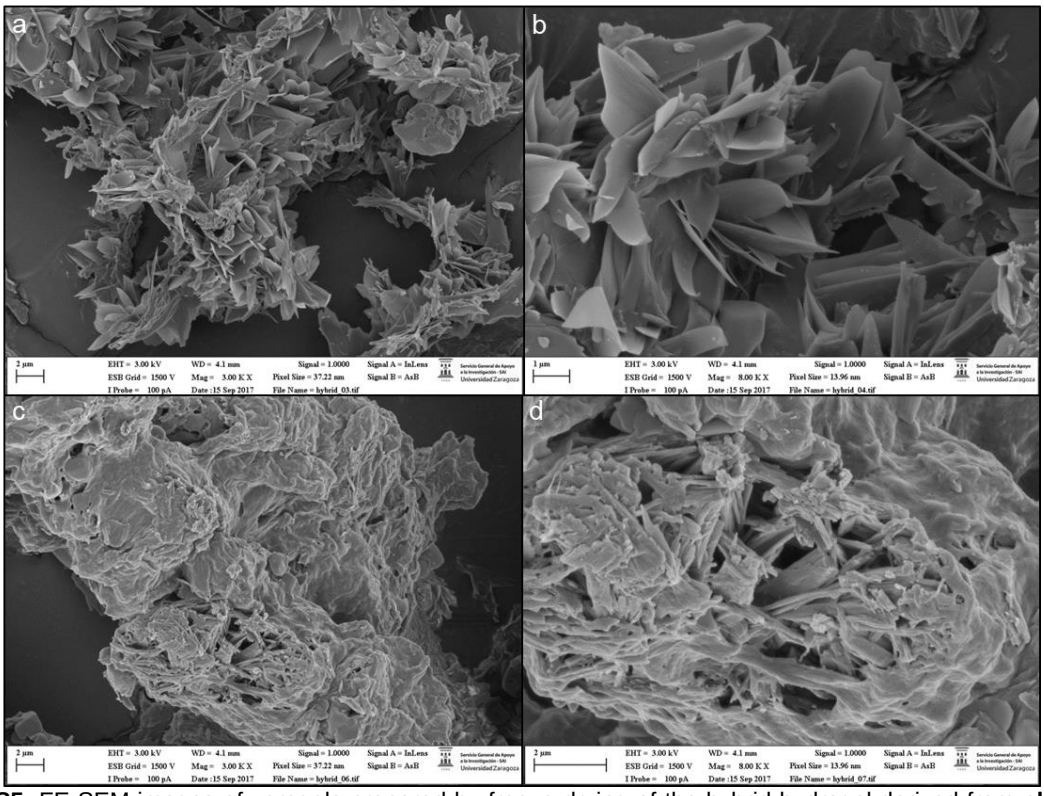


Figure S5. FE-SEM images of xerogels prepared by freeze-drying of the hybrid hydrogel derived from **click-TIA** and **5-TIA** (molar ratio 1:0.2, overall concentration: c = 19 g L^{-1}).

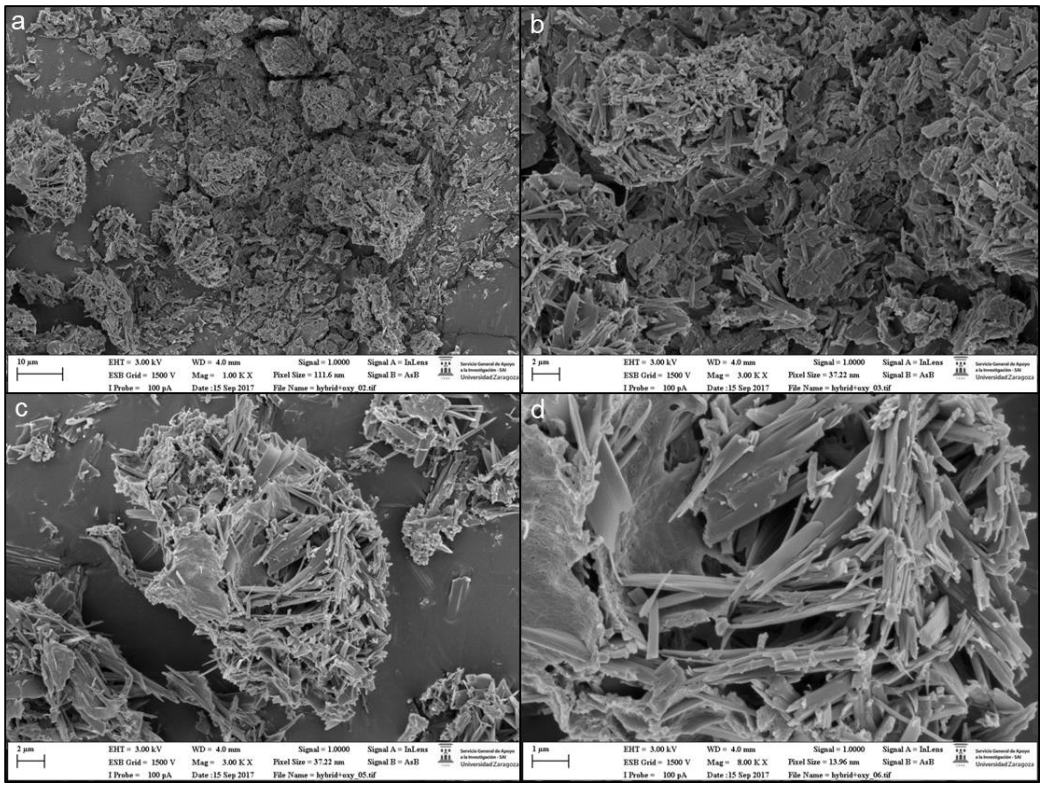


Figure S6. FE-SEM images of xerogels prepared by freeze-drying of the hybrid hydrogel derived from **click-TIA** and **5-TIA** (molar ratio 1:0.2, overall concentration: c = 19 g L^{-1}) and oxytetracycline hydrochloride (c = 0.8 g L^{-1}).

1.4. Drug release studies

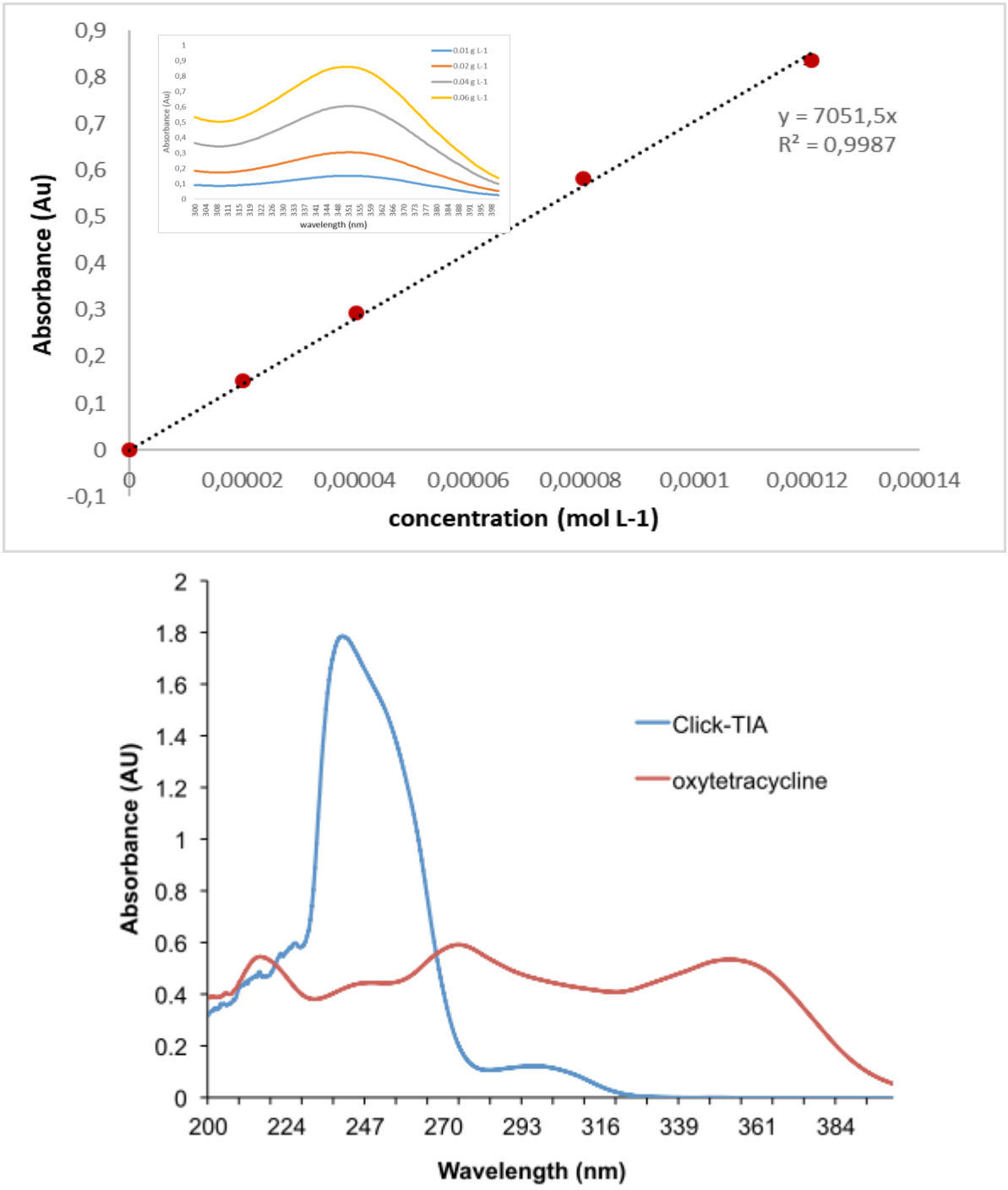


Figure S7. *Top:* Calibration curve of oxytetracycline hydrochloride in PBS buffer (0.01 M, pH 7.4) at the max. absorbance of the drug (λ_{max} = 353 nm). Each point was repeated in triplicate. *Bottom:* Overlapped spectra of gelator and drug.

The data obtained from the in vitro release experiments were fitted according to three drug release mathematical models, including first-order linear regression, Higuchi (eq. 1), Korsmeyer-Peppas (eq. 2) and Weibull (eq. 3) equation models. M_t and M_∞ values correspond to the cumulative and the maximal amounts of drug released at time *t*, respectively. In the case of the Higuchi equation model, the drug released fraction is proportional to the square root of time *t* in which *K* corresponds to the Higuchi constant. The Korsmeyer-Peppas equation model exponentially describes the relationship between the drug released fraction with the elapsed time *t*. *K* is a rate constant and *n* is the release exponent that describes the release processes governed in the liberation of a drug: In particular, there is a Fickian mechanism (Case I) when n is around 0.5 and anomalous diffusion (non-Fickian) when $0.5 < n < 1$ (Case II). In the case of the Weibull distribution, *b* parameter describes the diffusion mechanism: a) Fickian when $b \leq 0.75$, and b) others complex release processes combined with diffusion mechanisms when $0.75 < b < 1$. First-order linear regression provided the best fitting to the experimental data.

$$\frac{M_t}{M_\infty} = K \times \sqrt{t} \qquad \text{(Eq. 1)}$$

$$\frac{M_t}{M_\infty} = K \times t^n \qquad \text{(Eq. 2)}$$

$$\frac{M_t}{M_\infty} = \propto \times (1 - \exp(-(kt)^b)) \qquad \text{(Eq. 3)}$$

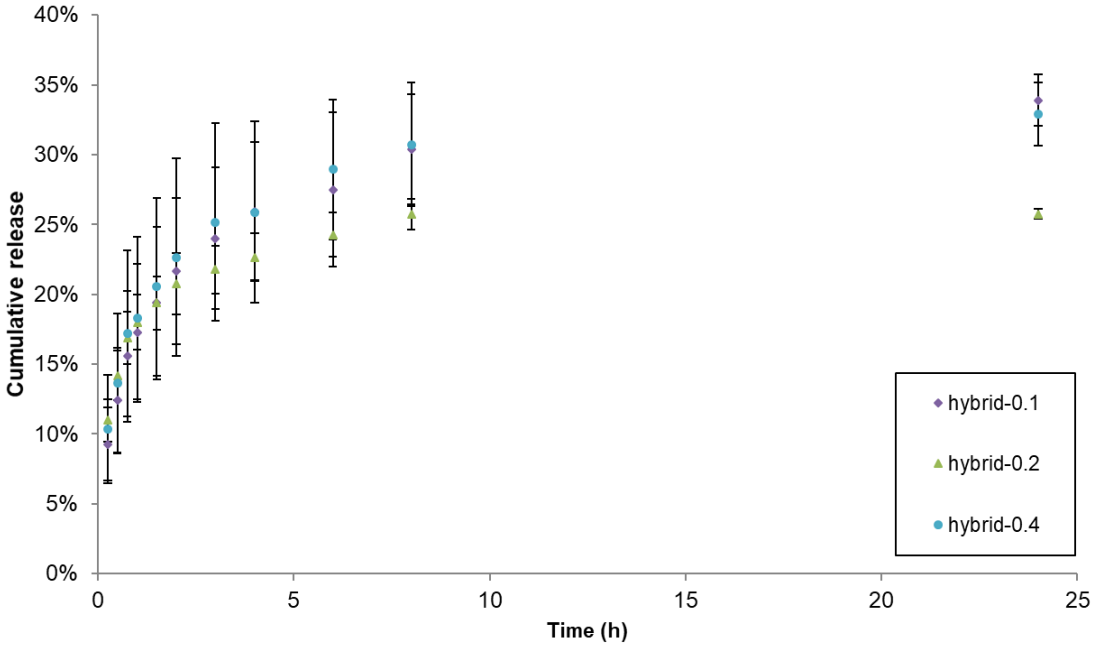


Figure S8. Drug release of oxytetracycline hydrochloride (c = 0.8 g L^{-1}) from hydrogels derived from hybrid hydrogels with varying **click-TIA**:**5-TIA** ratios (molar ratio 1:0.1-0.4, overall concentration: c = 19 g L^{-1}) at pH 7.4.

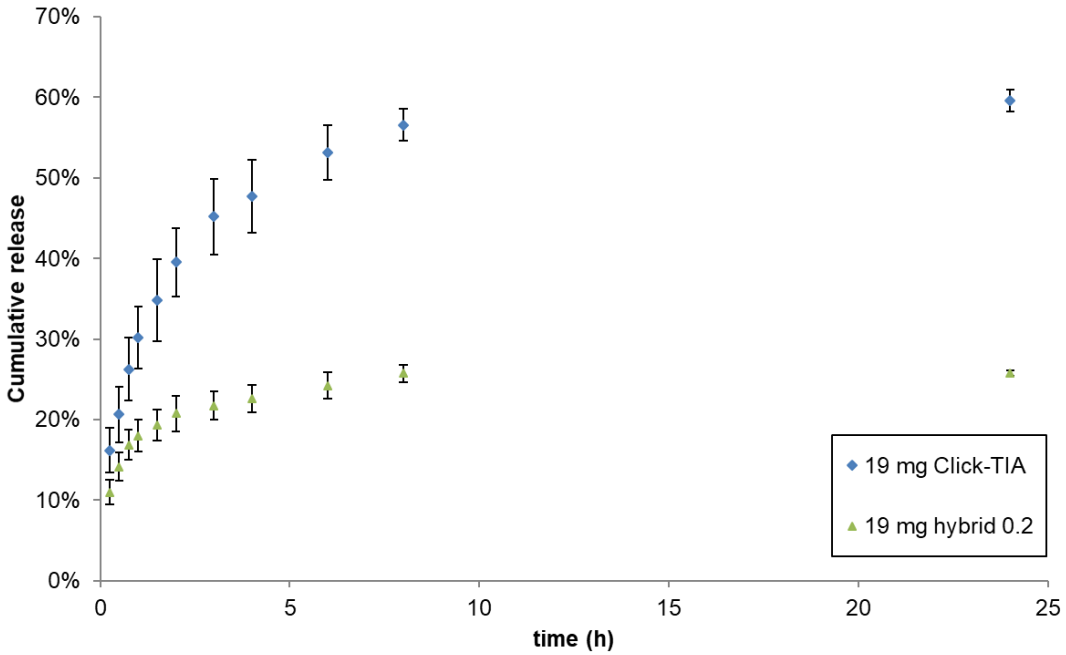


Figure S9. Drug release of oxytetracycline hydrochloride (c = 0.8 g L^{-1}) from hydrogels derived from **click-TIA** (c = 19 or 25 g L^{-1}).

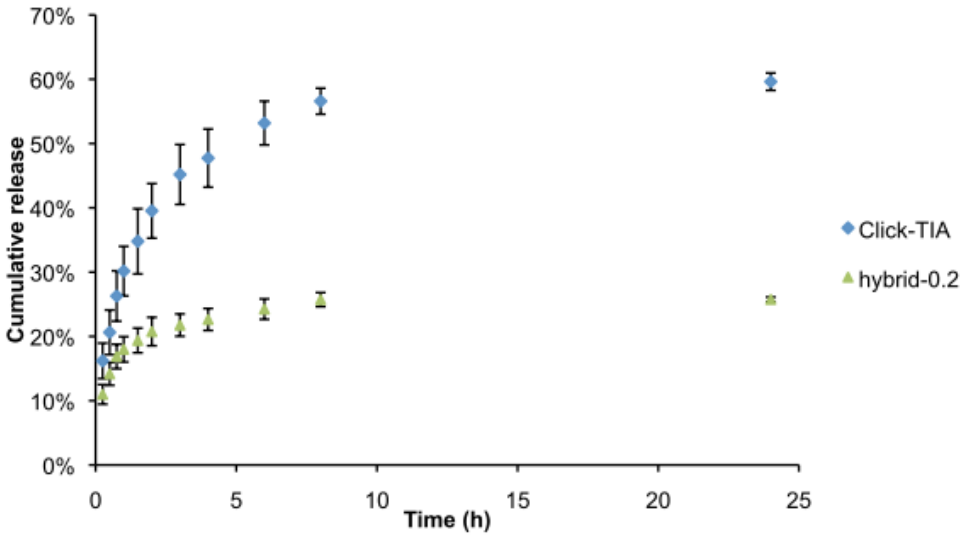
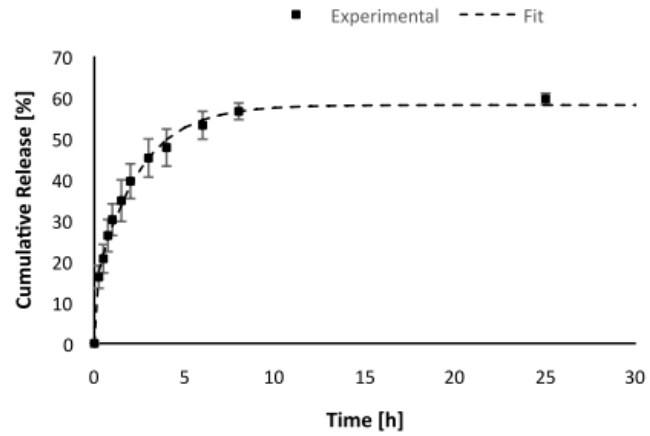
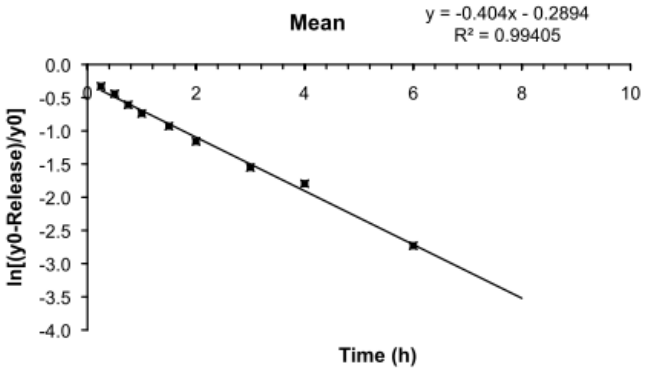


Figure S10. Drug release of oxytetracycline hydrochloride (c = 0.8 g L^{-1}) from hydrogels derived from **click-TIA** (c = 19 g L^{-1}) and hybrid made of **click-TIA**:**5-TIA** (molar ratio = 1:0.2) at pH 7.4.

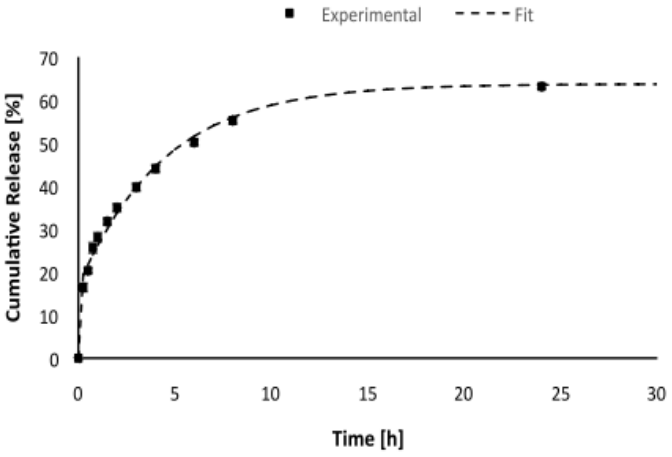
1-Click-TIA: 19 mg **Click-TIA** + 0.8 mg oxytetracycline, release at **pH 7.4**



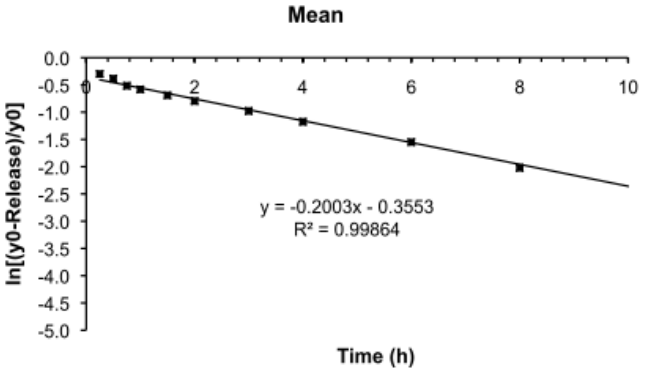
Fitting eq.	Parameters		
y = y0 + A * exp(R0 * x)	y0	A	R0
	58,09309343	-45,004025	-0,42009963



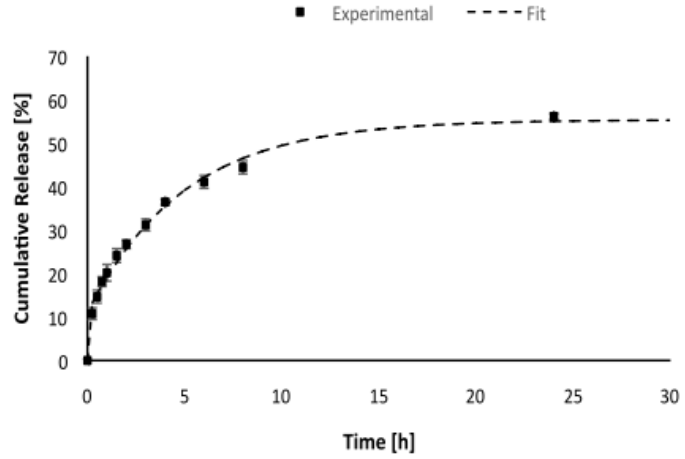
2-Click-TIA: 19 mg **Click-TIA** + 0.8 mg oxytetracycline, release at **pH 1.2**



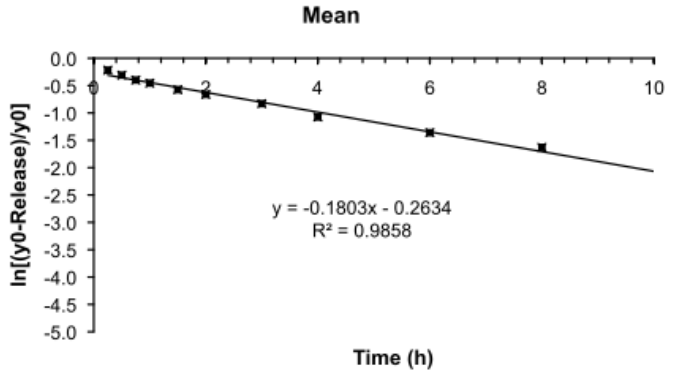
Fitting eq.	Parameters		
y = y0 + A * exp(R0 * x)	y0	A	R0
	63,71631114	-47,01455	-0,22584361



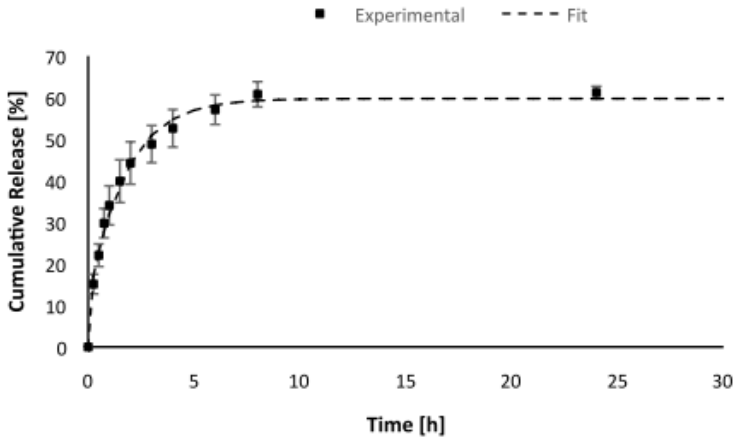
3-Click-TIA: 19 mg **Click-TIA** + 0.8 mg oxytetracycline, release at **pH 5.0**



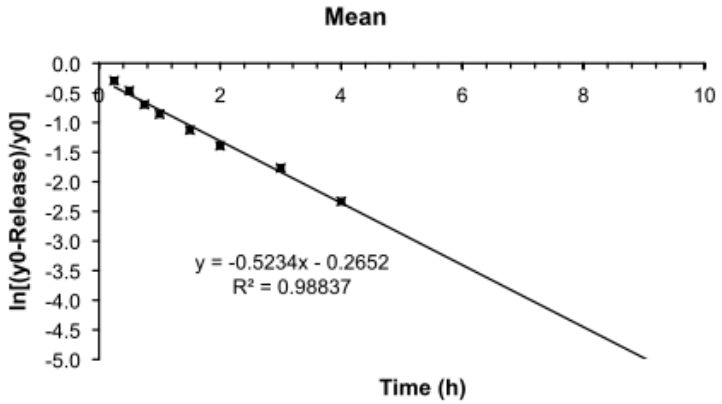
Fitting eq.	Parameters		
	y0	A	R0
y = y0 + A * exp(R0 * x)	55,36130005	-44,266684	-0,201319082



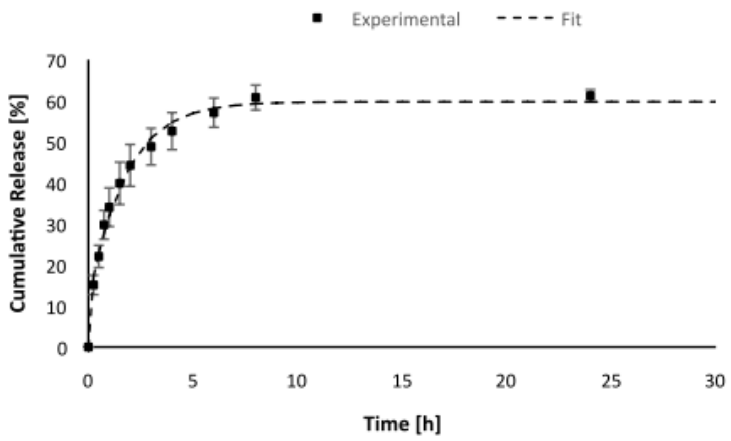
4-Click-TIA: 19 mg **Click-TIA** + 0.8 mg oxytetracycline, release at **pH 6.5**



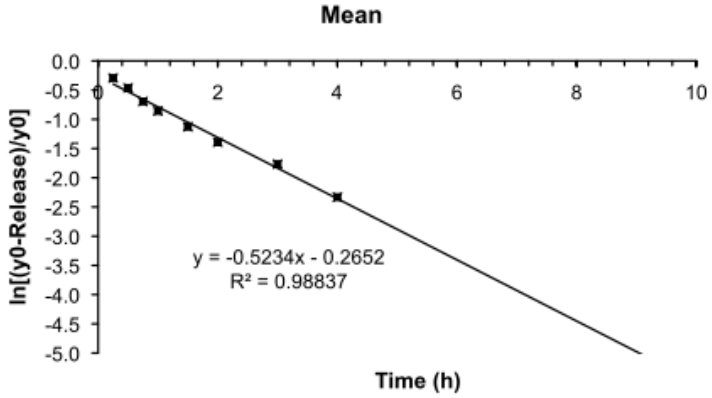
Fitting eq.	Parameters		
	y0	A	R0
y = y0 + A * exp(R0 * x)	54,55694762	-41,689978	-0,377490657



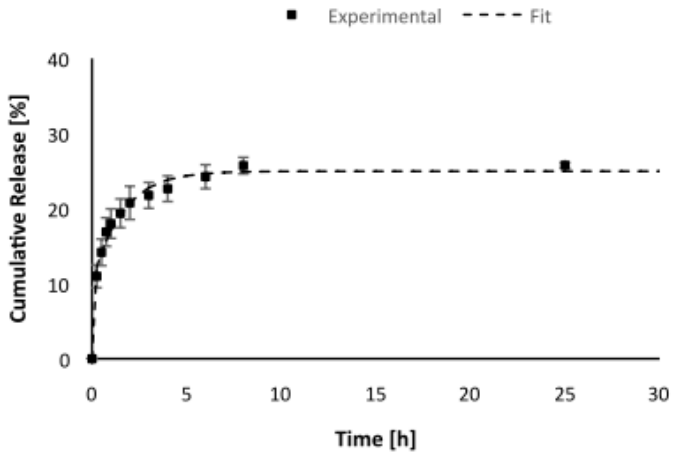
5-Click-TIA: 19 mg **Click-TIA** + 0.8 mg oxytetracycline, release at **pH 10**



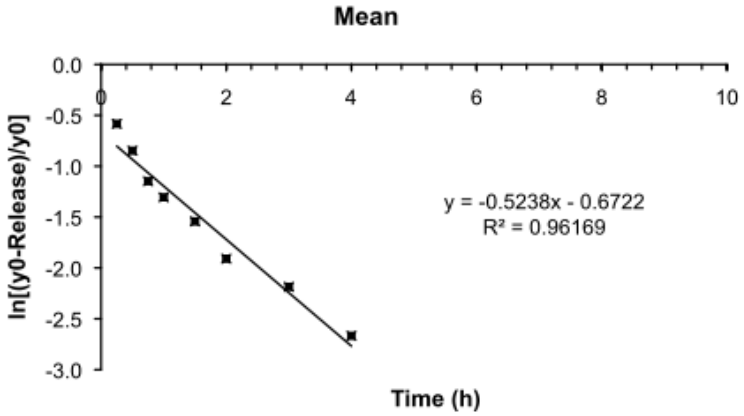
Fitting eq.	Parameters		
y = y0 + A * exp(R0 * x)	y0	A	R0
	59,73101516	-49,193354	-0,573677837



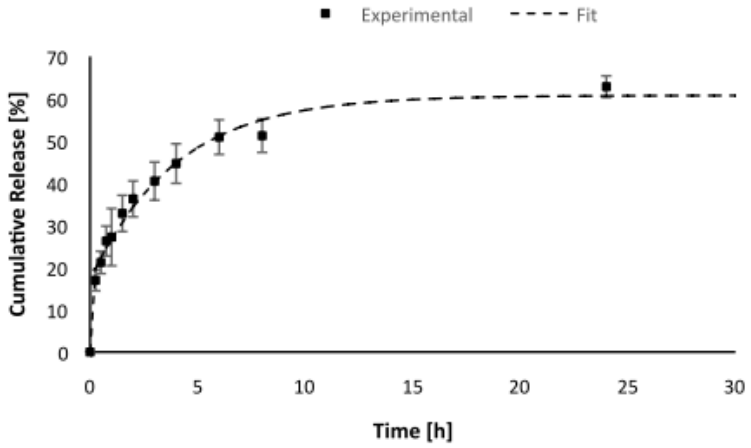
1-Hybrid: 19 mg **hybrid-0.2**+ 0.8 mg oxytetracycline, release at **pH 7.4**



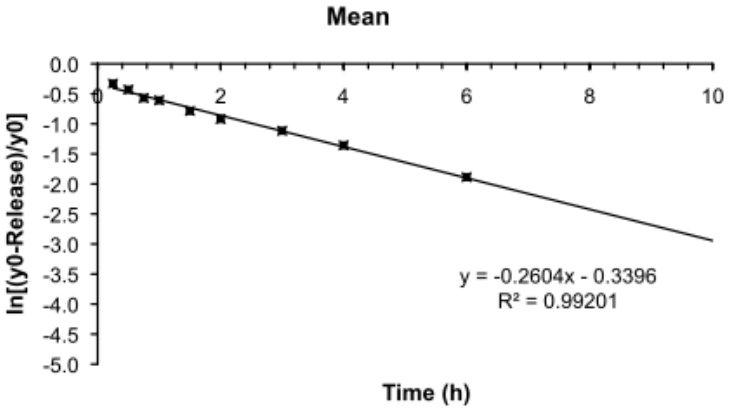
Fitting eq.	Parameters		
y = y0 + A * exp(R0 * x)	y0	A	R0
	24,97119486	-14,991524	-0,642156061



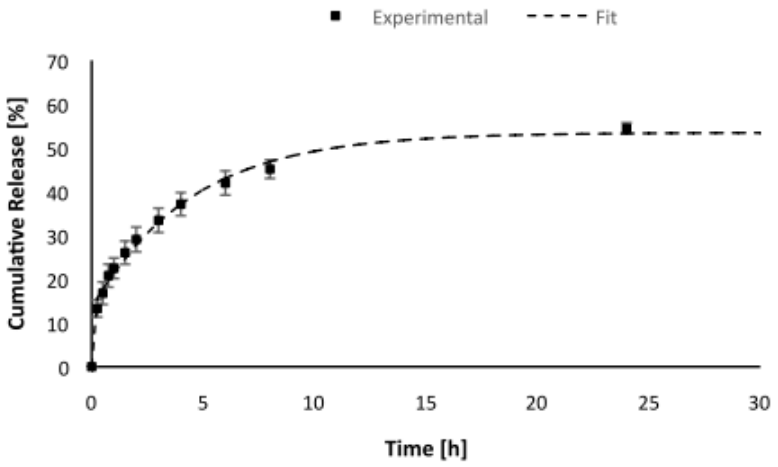
2-Hybrid: 19 mg **hybrid-0.2** + 0.8 mg oxytetracycline, release at **pH 1.2**



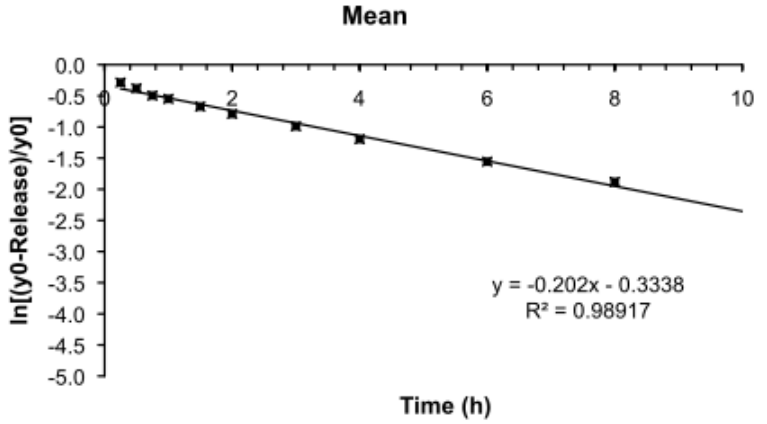
Fitting eq.	Parameters		
y = y0 + A * exp(R0 * x)	y0	A	R0
	60,75507799	-43,689672	-0,253240843



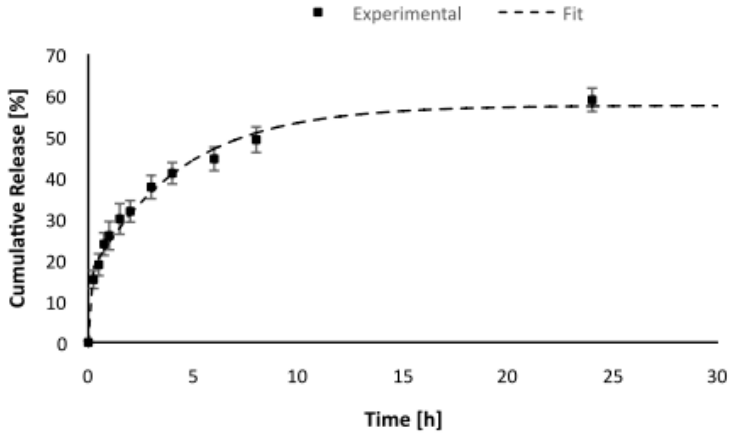
3-Hybrid: 19 mg **hybrid-0.2**+ 0.8 mg oxytetracycline, release at **pH 5.0**



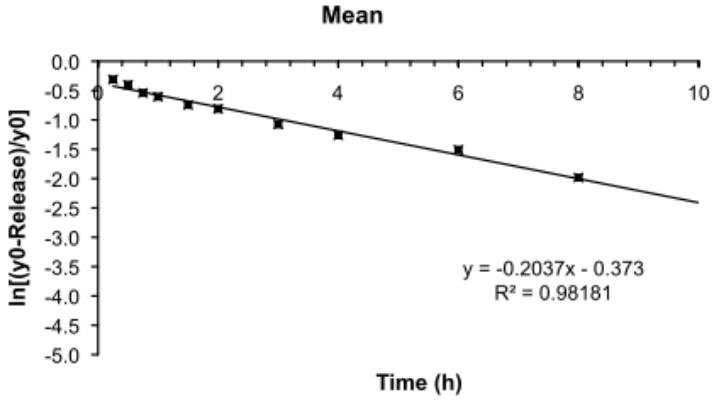
Fitting eq.	Parameters		
y = y0 + A * exp(R0 * x)	y0	A	R0
	53,46945307	-40,048262	-0,224866412



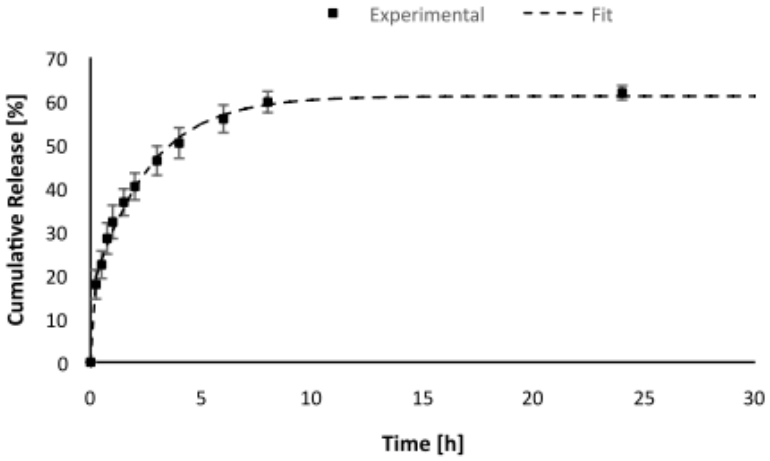
4-Hybrid: 19 mg **hybrid-0.2** + 0.8 mg oxytetracycline, release at **pH 6.5**



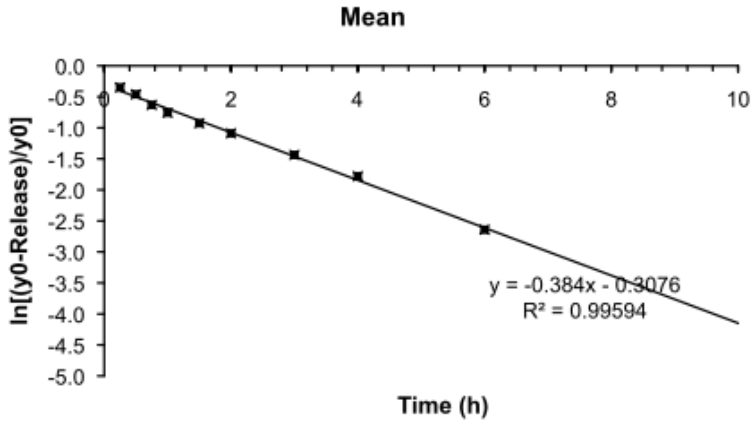
Fitting eq.	Parameters		
y = y0 + A * exp(R0 * x)	y0	A	R0
	57,50537172	-41,701596	-0,230139676



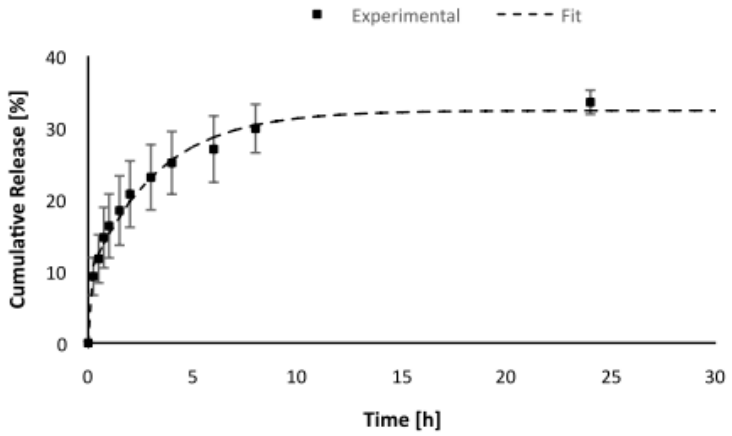
5-Hybrid: 19 mg **hybrid-0.2**+ 0.8 mg oxytetracycline, release at **pH 10.0**



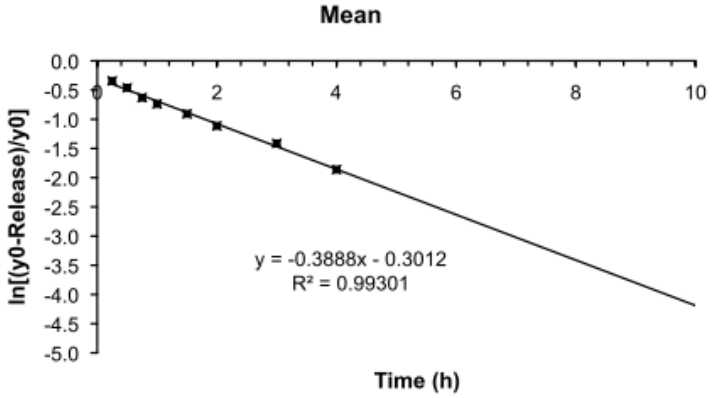
Fitting eq.	Parameters		
y = y0 + A * exp(R0 * x)	y0	A	R0
	61,0956058	-45,889662	-0,39574179



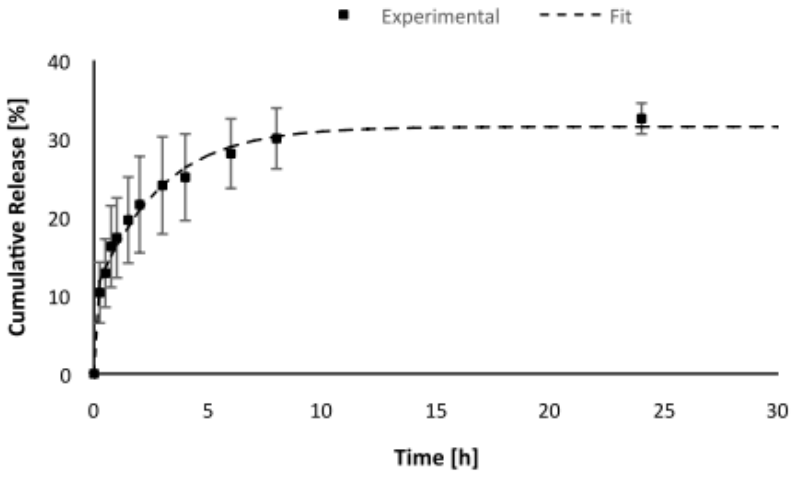
6-Hybrid: 19 mg **hybrid-0.1** mg + 0.8 mg oxytetracycline, release at **pH 7.4**



Fitting eq.	Parameters		
y = y0 + A * exp(R0 * x)	y0	A	R0
	32,38519163	-23,279773	-0,305904267



7-Hybrid: 19 mg **hybrid-0.4** mg + 0.8 mg oxytetracycline, release at **pH 7.4**



Fitting eq.	Parameters		
y = y0 + A * exp(R0 * x)	y0	A	R0
	31,51949119	-21,543308	-0,355440837

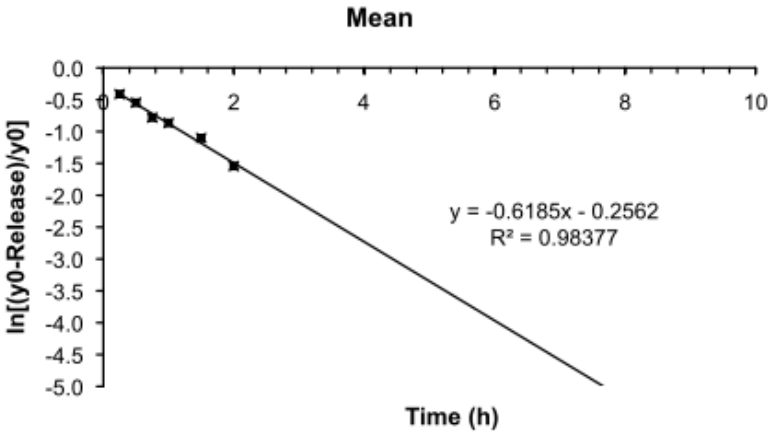


Figure S11. Drug release profiles and linear regression fitting curves. Conditions for the preparation of drug-loaded gels are specified in each case. Note: Release models have been applied to all data points.

Table S1. Correlation coefficients obtained by fitting the experimental data with Higuchi, Korsmeyer-Peppas and Weibull models.

Gel formulation	Drug release mathematical models		
	Higuchi	Korsmeyer-Peppas	Weibull
1-Click-TIA: 19 mg Click-TIA + 0.8 mg oxytetracycline, release at pH 7.4	$R^2 = 0.71886$	$R^2 = 0.98081$	$R^2 = 0.98737$
2-Click-TIA: 19 mg Click-TIA + 0.8 mg oxytetracycline, release at pH 1.2	$R^2 = 0.77419$	$R^2 = 0.99551$	$R^2 = 0.99732$
3-Click-TIA: 19 mg Click-TIA + 0.8 mg oxytetracycline, release at pH 5.0	$R^2 = 0.99107$	$R^2 = 0.98014$	$R^2 = 0.99107$
4-Click-TIA: 19 mg Click-TIA + 0.8 mg oxytetracycline, release at pH 6.5	$R^2 = 0.79926$	$R^2 = 0.93465$	$R^2 = 0.95558$
5-Click-TIA: 19 mg Click-TIA + 0.8 mg oxytetracycline, release at pH 10	$R^2 = 0.70992$	$R^2 = 0.86849$	$R^2 = 0.89948$
1-Hybrid: 19 mg hybrid-0.2+ 0.8 mg oxytetracycline, release at pH 7.4	$R^2 = 0.64958$	$R^2 = 0.87776$	$R^2 = 0.94407$
2-Hybrid: 19 mg hybrid-0.2 + 0.8 mg oxytetracycline, release at pH 1.2	$R^2 = 0.77172$	$R^2 = 0.94627$	$R^2 = 0.98496$
3-Hybrid: 19 mg hybrid-0.2+ 0.8 mg oxytetracycline, release at pH 5.0	$R^2 = 0.87961$	$R^2 = 0.97916$	$R^2 = 0.98932$
4-Hybrid: 19 mg hybrid-0.2 + 0.8 mg oxytetracycline, release at pH 6.5	$R^2 = 0.86586$	$R^2 = 0.97552$	$R^2 = 0.98829$
5-Hybrid: 19 mg hybrid-0.2+ 0.8 mg oxytetracycline, release at pH 10.0	$R^2 = 0.76203$	$R^2 = 0.98688$	$R^2 = 0.99516$
6-Hybrid: 19 mg hybrid-0.1 mg + 0.8 mg oxytetracycline, release at pH 7.4	$R^2 = 0.81592$	$R^2 = 0.98556$	$R^2 = 0.9641$
7-Hybrid: 19 mg hybrid-0.4 + 0.8 mg oxytetracycline, release at pH 7.4	$R^2 = 0.76823$	$R^2 = 0.98283$	$R^2 = 0.98685$

1.5. NMR spectra

→ NMR spectra are found in the ESI of the paper.

2. Click-TIA metallogels

2.1. Role of water in gel formation

Table S2. Role of water in gel formation.

Entry	c(**click-TIA**)	c(CuA)	V(DMF)	V(H_2O)	Phase[b]
1	0.2 M	0.2 M	500 µL	-	G
2	0.2 M	0.2 M	475 µL	25 µL	G
3	0.2 M	0.2 M	450 µL	50 µL	G
4	0.2 M	0.2 M	400 µL	100 µL	G
5	0.2 M	0.2 M	350 µL	150 µL	G
6	0.2 M	0.2 M	300 µL	200 µL	G
7	0.2 M	0.2 M	250 µL	250 µL	P
8	0.2 M	0.2 M	200 µL	300 µL	P
9	0.2 M	0.2 M	150 µL	350 µL	P
10	0.2 M	0.2 M	100 µL	400 µL	P
11	0.2 M	0.2 M	50 µL	450 µL	P
12	0.2 M	0.2 M	25 µL	475 µL	P
13	0.2 M	0.2 M	-	500 µL	P

[a] Abbreviations: G = gel; PG = partial gel; P = precipitate; S = solution.

2.2. Oscillatory rheology

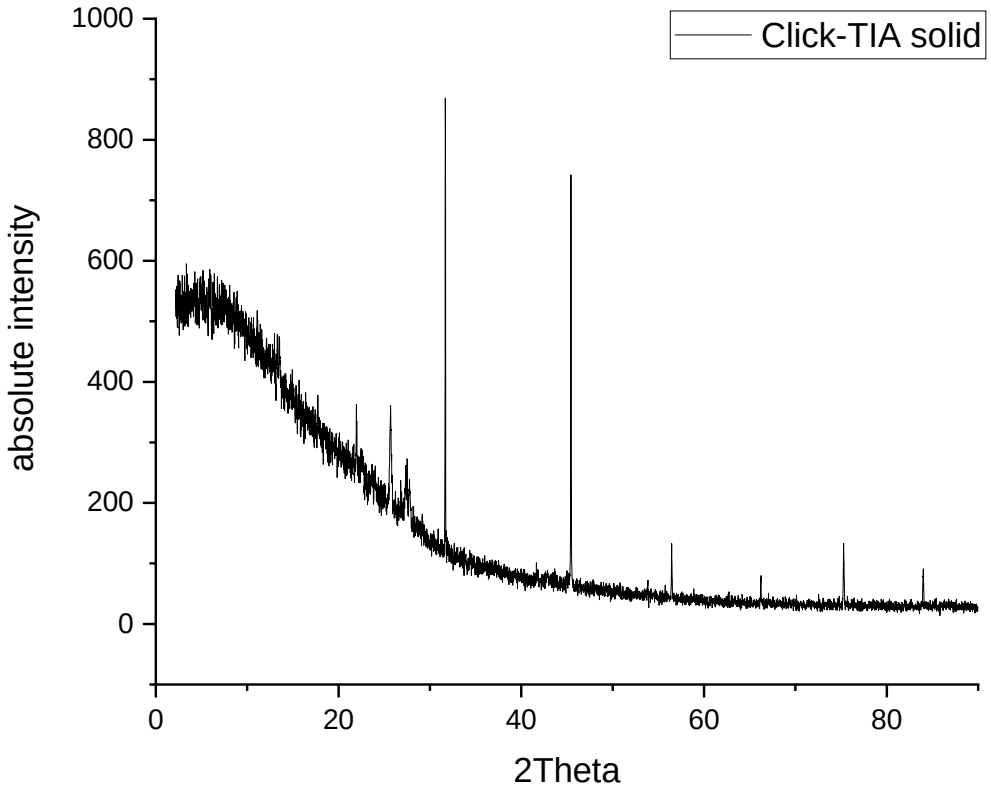
Table S3. Rheological properties of [CuA + **click-TIA**] metallogels-**1**, -**2**, and -**3**.[a]

Metallogel	c(**click-TIA**)	c(CuA)	*G′* (Pa)	*G″* (Pa)	tan δ	γ (%)
1	0.2 M	0.1 M	13	2	0.166 ± 0.01	16
2	0.2 M	0.2 M	960	97	0.100 ± 0.01	80
3	0.2 M	0.3 M	1810	212	0.112 ± 0.01	32

[a]Rheological measurements were performed at 1 Hz frequency and 0.1% strain.

2.3. PXRD

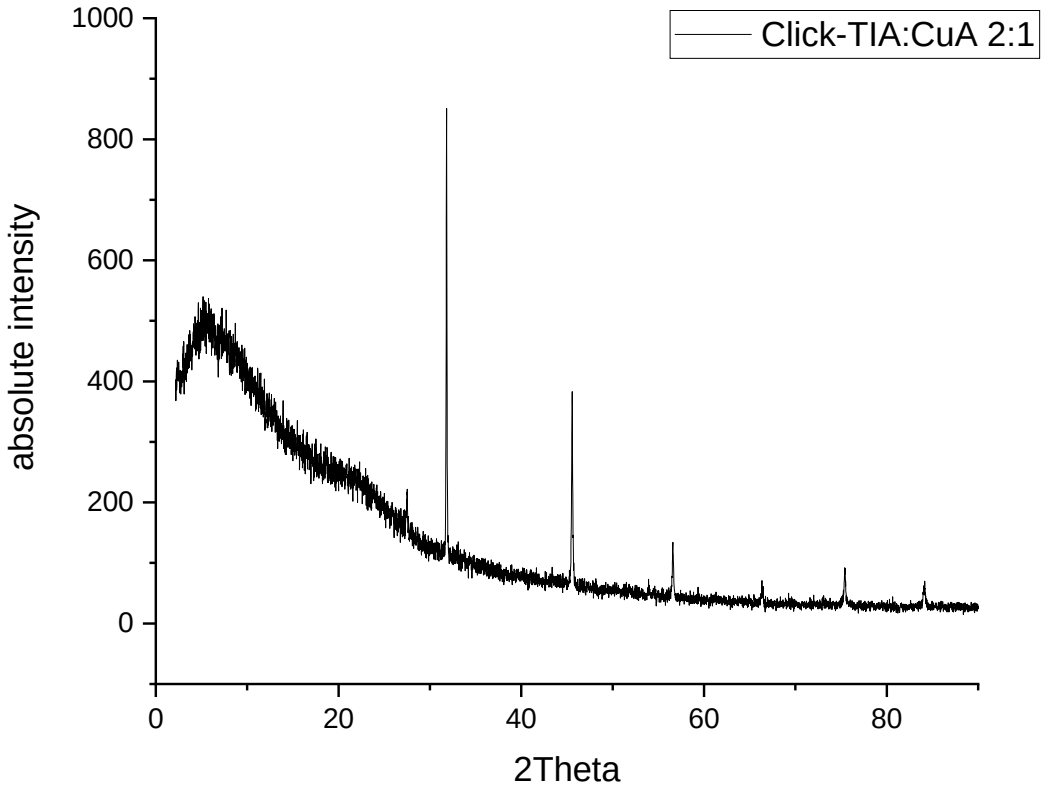
a)



Click-TIA solid

2θ (°)	θ	d (nm)
21,95	10,975	4,04655474
25,7	12,85	3,46396625
27,35	13,675	3,258616
27,515	13,7575	3,23944821
27,77	13,885	3,21027777
31,685	15,8425	2,82196972
45,44	22,72	1,99459848
56,45	28,225	1,62888774
66,245	33,1225	1,40977766
75,275	37,6375	1,26146823
83,99	41,995	1,15133378

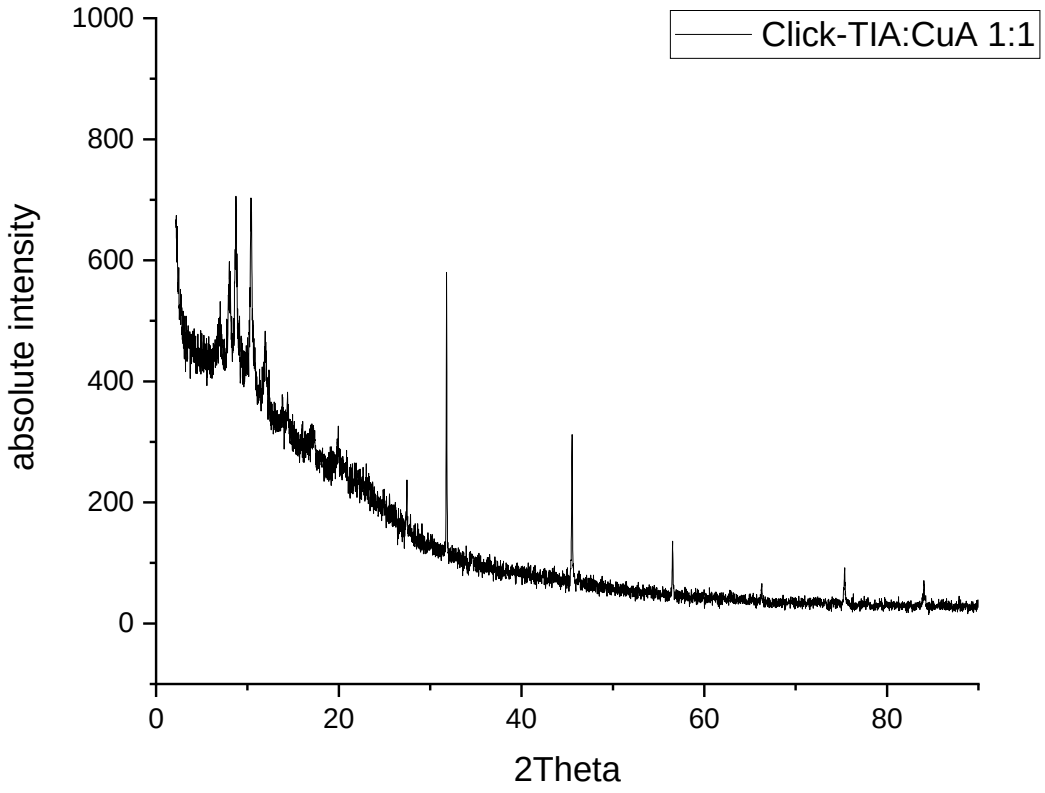
b)



Metallogel-**1**

2θ (°)	θ	d (nm)
27,515	13,7575	3,23944821
31,82	15,91	2,81030424
45,575	22,7875	1,98900333
56,585	28,2925	1,62532122
66,335	33,1675	1,40808286
75,425	37,7125	1,25933124
84,155	42,0775	1,14949597

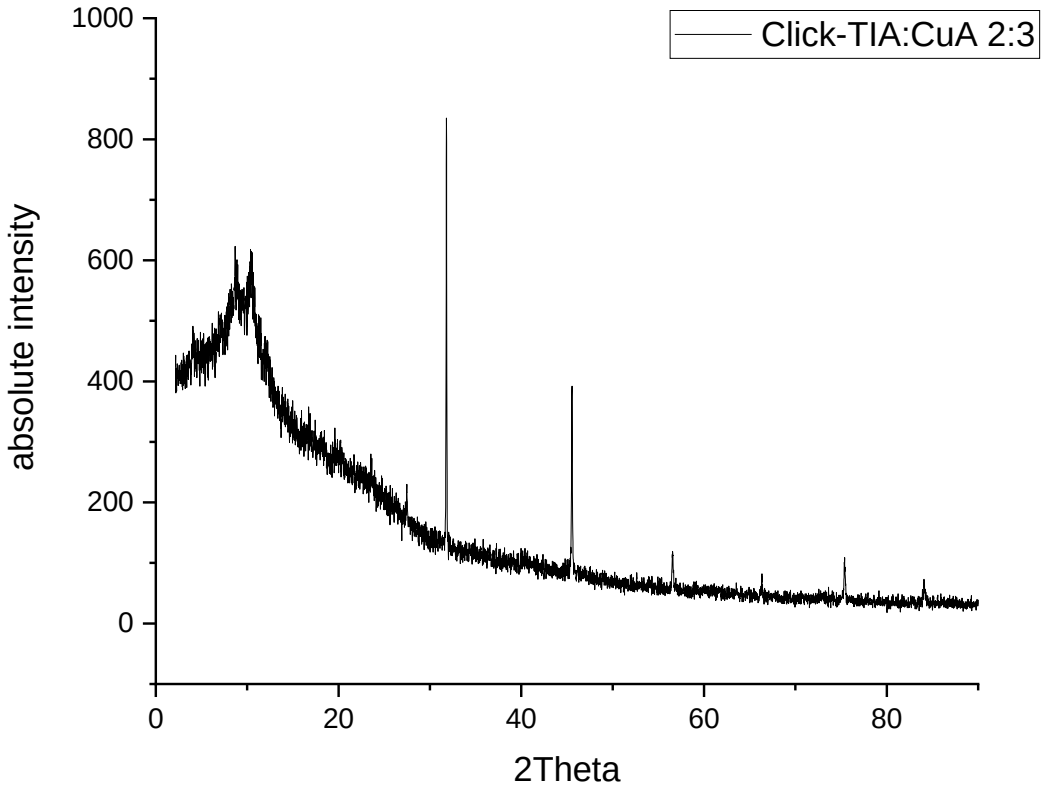
c)



Metallogel-**2**

2θ (°)	θ	d (nm)
2,18	1,09	40,49797
7,025	3,5125	12,5744512
8,015	4,0075	11,0233566
8,75	4,375	10,098973
10,385	5,1925	8,51238233
11,945	5,9725	7,40394891
19,94	9,97	4,44969352
27,455	13,7275	3,24639139
31,79	15,895	2,81288789
45,53	22,765	1,99086458
56,525	28,2625	1,62690413
66,29	33,145	1,40892964
75,365	37,6825	1,26018491
84,035	42,0175	1,15083174

d)



Metallogel-**3**

2θ (°)	θ	d (nm)
8,69	4,345	10,1685662
10,37	5,185	8,52466166
27,47	13,735	3,24465272
31,805	15,9025	2,81159545
45,545	22,7725	1,99024375
56,555	28,2775	1,62611223
66,335	33,1675	1,40808286
75,38	37,69	1,25997135
84,08	42,04	1,15033031

e)

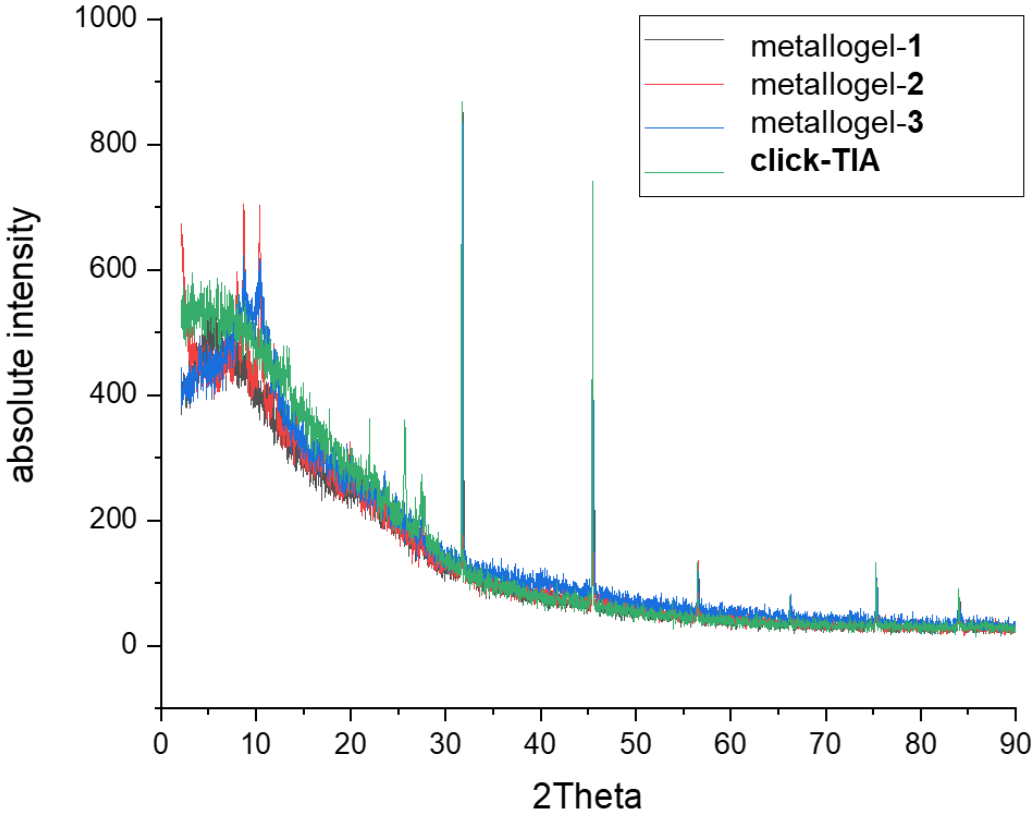


Figure S12. PXRD patterns and lattice spacings of a) **click-TIA** powder, b) xerogel of metallogel-**1** (*i.e.***click-TIA**:CuA 0.2 M:0.1 M), c) xerogel of metallogel-**2** (*i.e.***click-TIA**:CuA 0.2 M:0.2 M), d) xerogel of metallogel-**3** (*i.e.***click-TIA**:CuA 0.2 M:0.3 M); e) 0verlap spectra of a)-d).

2.4. Additional FE-SEM images

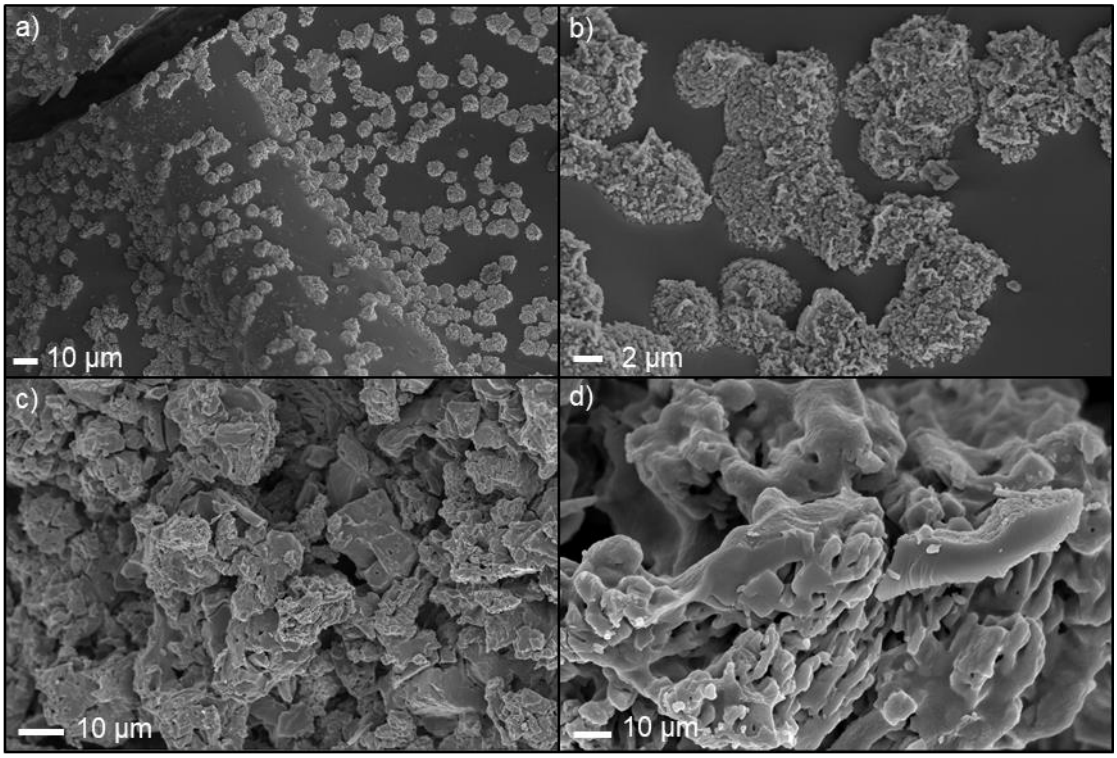


Figure S13. FE-SEM images of xerogels prepared by freeze-drying of metallogel-**1** (*i.e.* **click-TIA**:CuA 0.2 M:0.1 M).

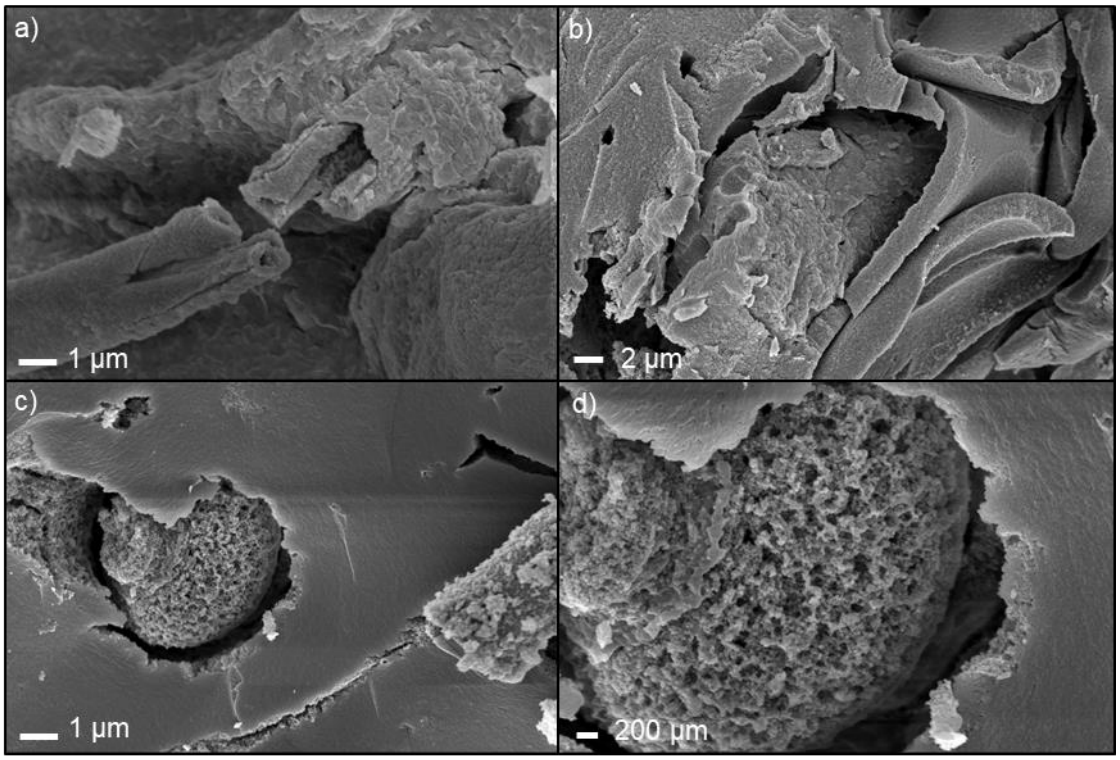


Figure S14. FE-SEM images of xerogels prepared by freeze-drying of metallogel-**2** (*i.e.* **click-TIA**:CuA 0.2 M:0.2 M).

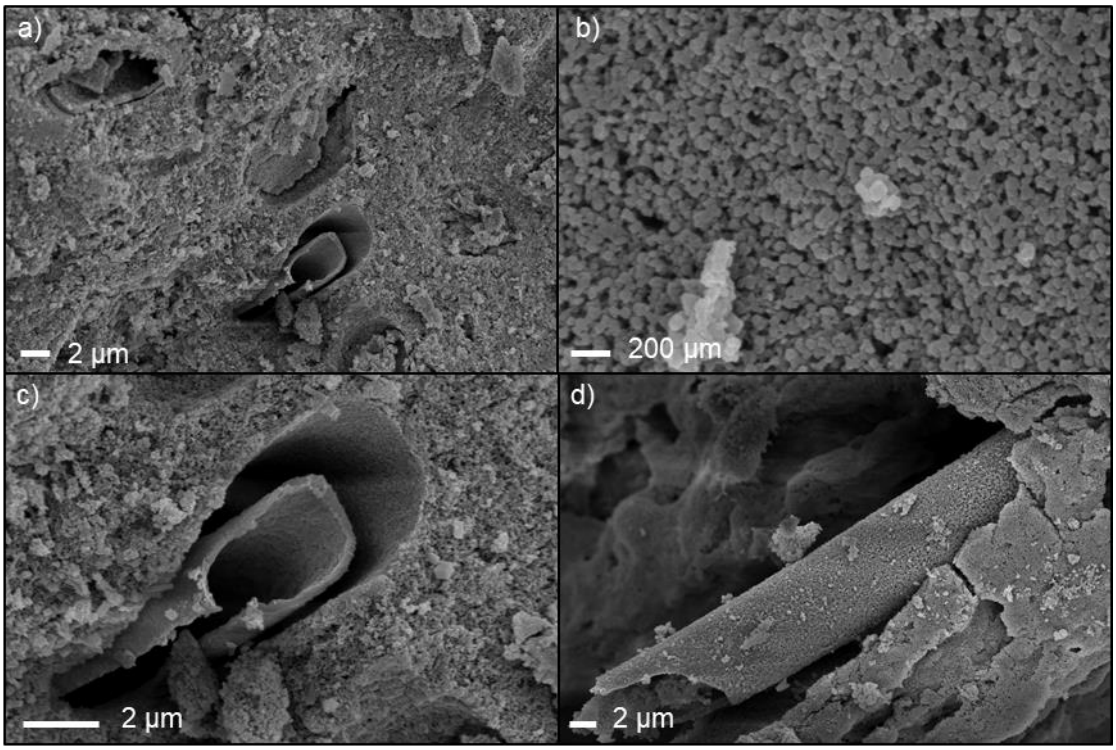


Figure S15. FE-SEM images of xerogels prepared by freeze-drying of metallogel-**3** (*i.e.* **click-TIA**:CuA 0.2 M:0.3 M).