

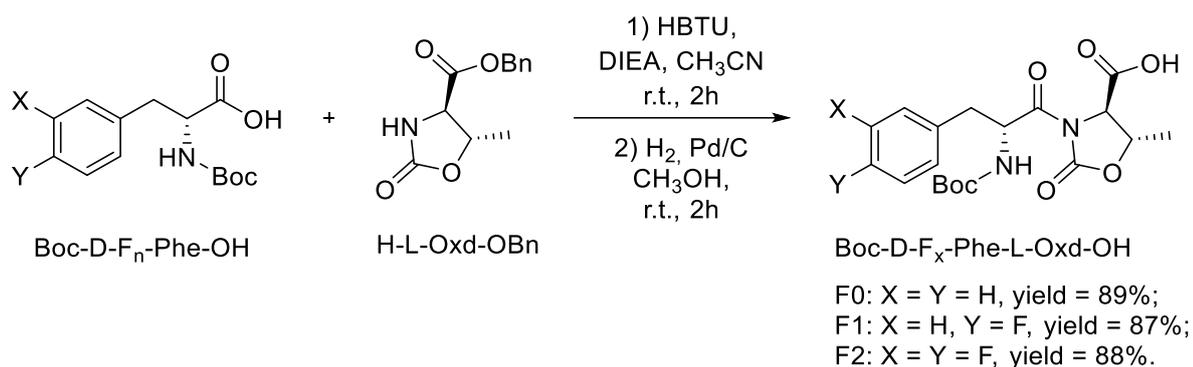
Supporting Information

Fluorine Effect in the Gelation Ability of Low Molecular Weight Gelators

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Scheme S1. Reagents and conditions: 1) Boc-D-F_n-Phe-OH (1.0 eq), H-L-Oxd-OBn (1.0 eq), HBTU (1.1 eq), DIEA (2.2 eq) in CH₃CN (concentration of the first two reagents is 0.1 M) for 2 h at r.t.. 2) Boc-D-F_n-Phe-L-Oxd-OBn (1.0 eq) and Pd/C (10% w/w) in CH₃OH (concentration of the first reagent is 10 mg/mL) for 2 h at r.t. under H₂ atmosphere.

Characterization of compounds F0, F1 and F2

Boc-D-Phe-L-Oxd-OH, F0

Characterisation matched literature values. See ref. [1].

Boc-D-F₁Phe-L-Oxd-OH, F1

The product **F1** is obtained as a white solid with an 87% yield. M.p. = 172-178°C; $[\alpha]_{D^{25}} = -32.2^{\circ}$ (c = 0.5 in CH₃OH); IR (ATR-IR): ν 3370, 3364, 2984, 2937, 1778, 1720, 1687, 1603, 1510 cm⁻¹; ¹H NMR (CD₃OD, 400 MHz): δ 1.31 (9H, s, CH₃ *t*-Bu), 1.47 (3H, d, J = 6.4 Hz, CH₃ Oxd), 2.71 (1H, dd, J = 10.0, 13.2 Hz, CH benzyl), 3.10 (1H, m, CH benzyl), 4.41 (1H, d, J = 3.6 Hz, C α H Oxd), 4.69 (1H, m, C β H Oxd), 5.63 (1H, dd, J = 4.0, 9.6 Hz, C α H F-Phe), 6.97 (2H, m, CH Ar), 7.30 (2H, m, CH Ar); ¹³C (CD₃OD₃, 100 MHz): δ 19.77, 27.18, 37.19, 54.37, 61.92, 74.57, 79.04, 114.32, 114.53, 130.85, 130.93, 132.88, 152.28, 155.89, 163.07, 170.04, 172.44; ¹⁹F NMR (CD₃OD, 376.5 MHz): δ -118.63, -118.46.

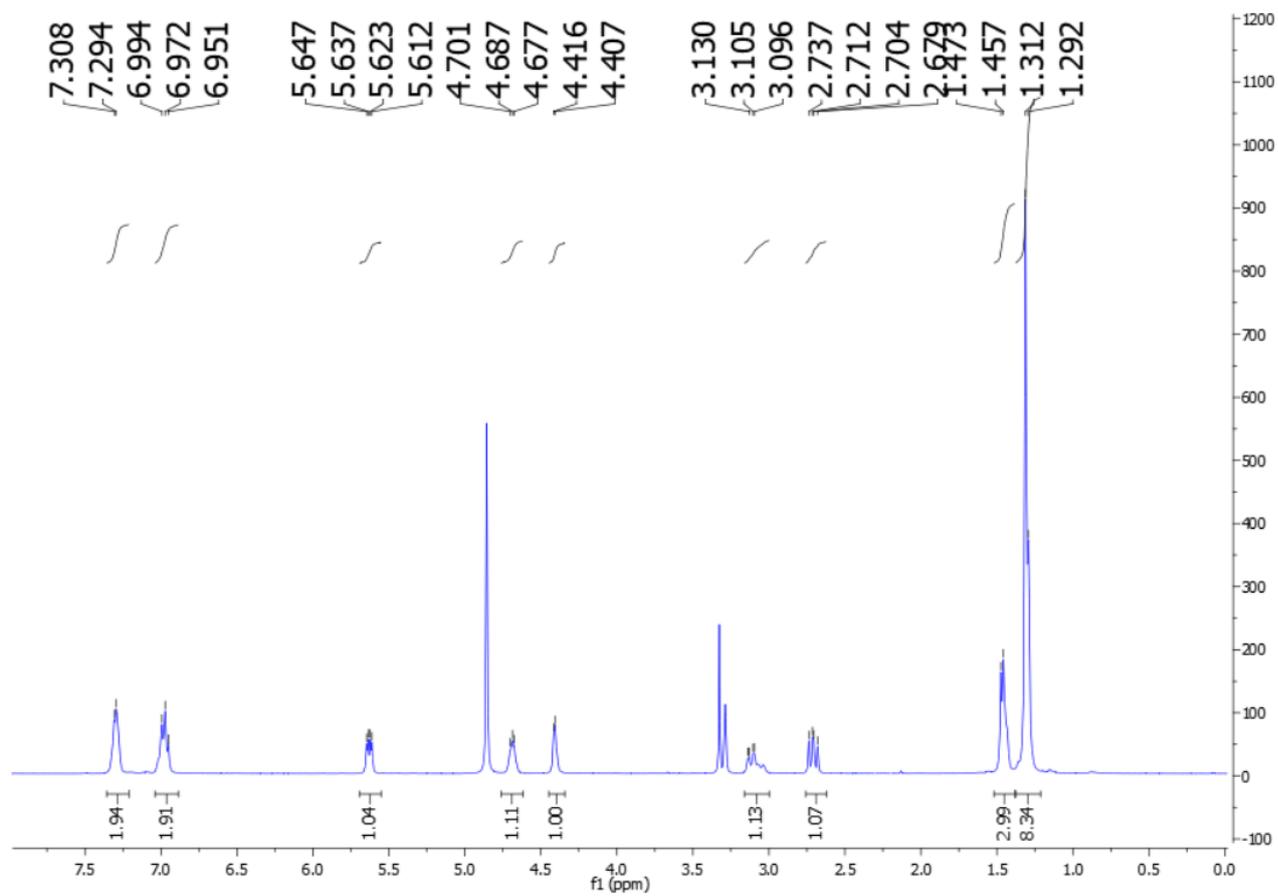
Boc-D-F₂Phe-L-Oxd-OH, F0

Characterisation matched literature values. See ref. [2].

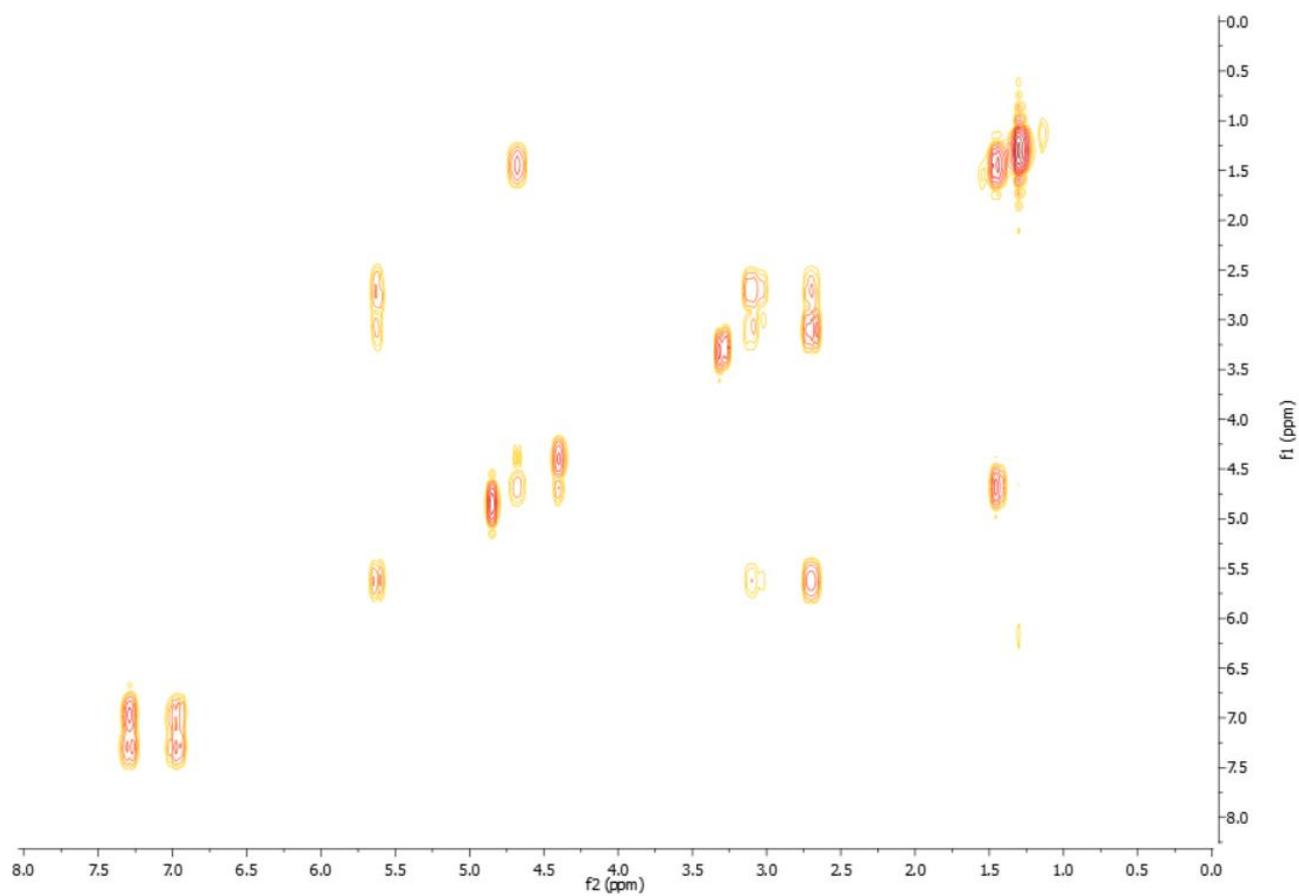
References

1. Milli, L.; Castellucci, N.; Tomasini, C. Turning around the L-Phe-D-oxd moiety for a versatile low-molecular-weight gelator. *European J. Org. Chem.* **2014**, 2014, 5954–5961, doi:10.1002/ejoc.201402787.
2. Ravarino, P.; Giuri, D.; Faccio, D.; Tomasini, C. Designing a transparent and fluorine containing hydrogel. *Gels* **2021**, 7, 1–10, doi:10.3390/gels7020043.

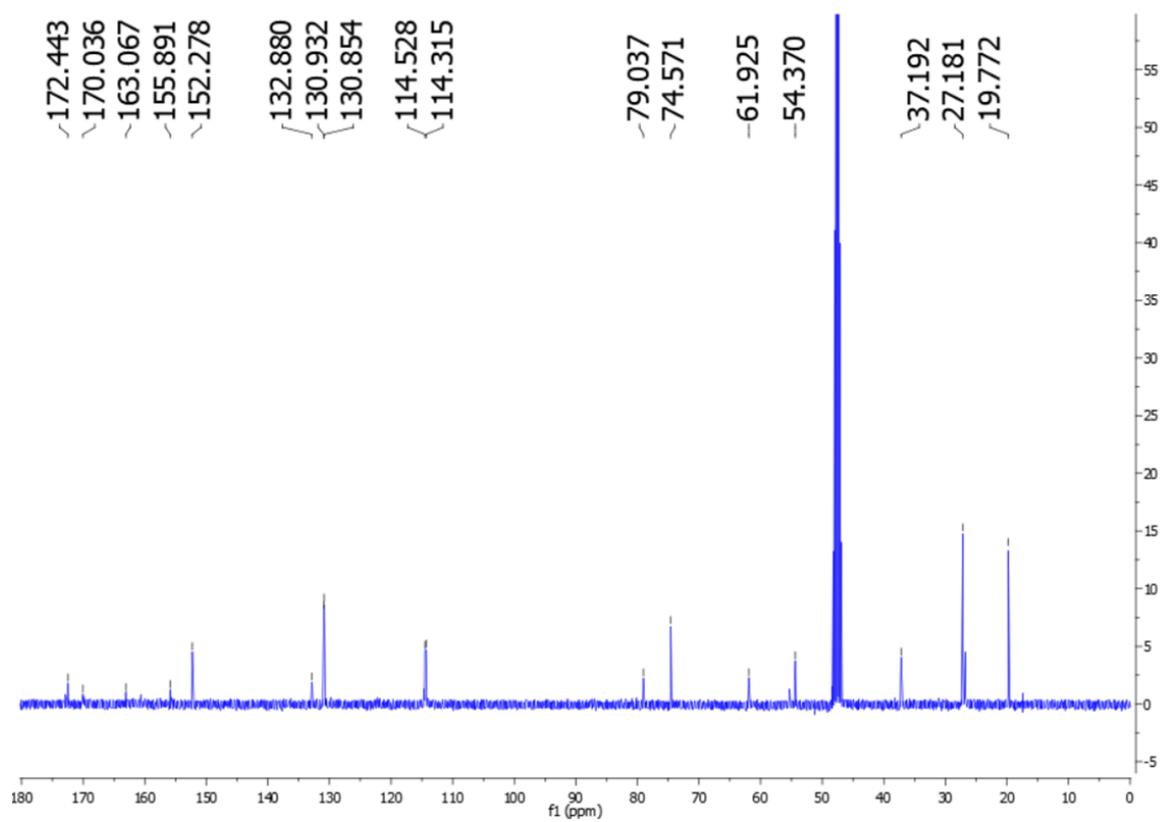
^1H NMR spectrum of compound F1, acquired in CD_3OD



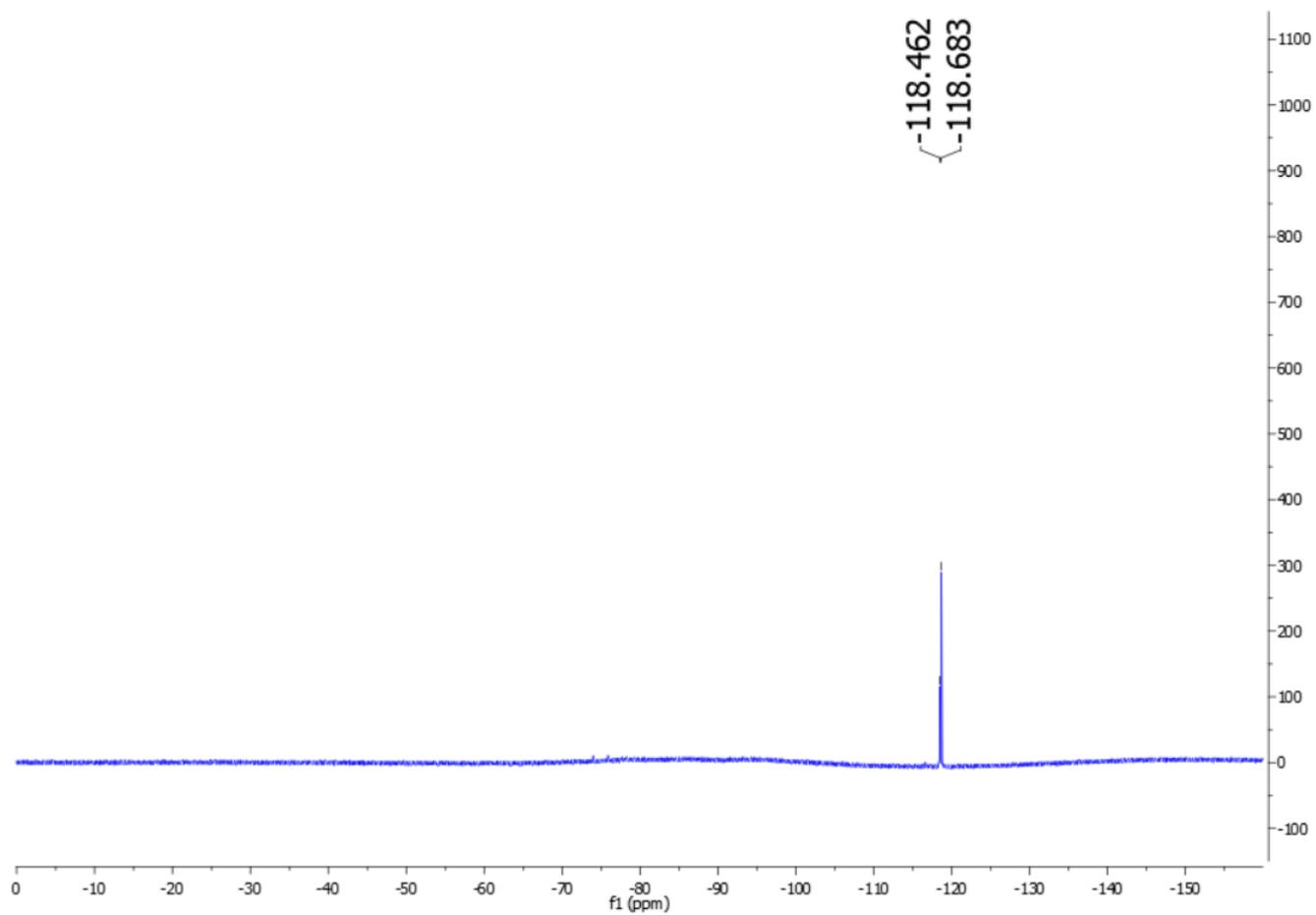
COSY NMR spectrum of compound **F1**, acquired in CD₃OD



^{13}C NMR spectrum of compound F1, acquired in CD_3OD .



^{19}F NMR spectrum of compound **F1**, acquired in CD_3OD



ATR-IR spectrum of compound F1

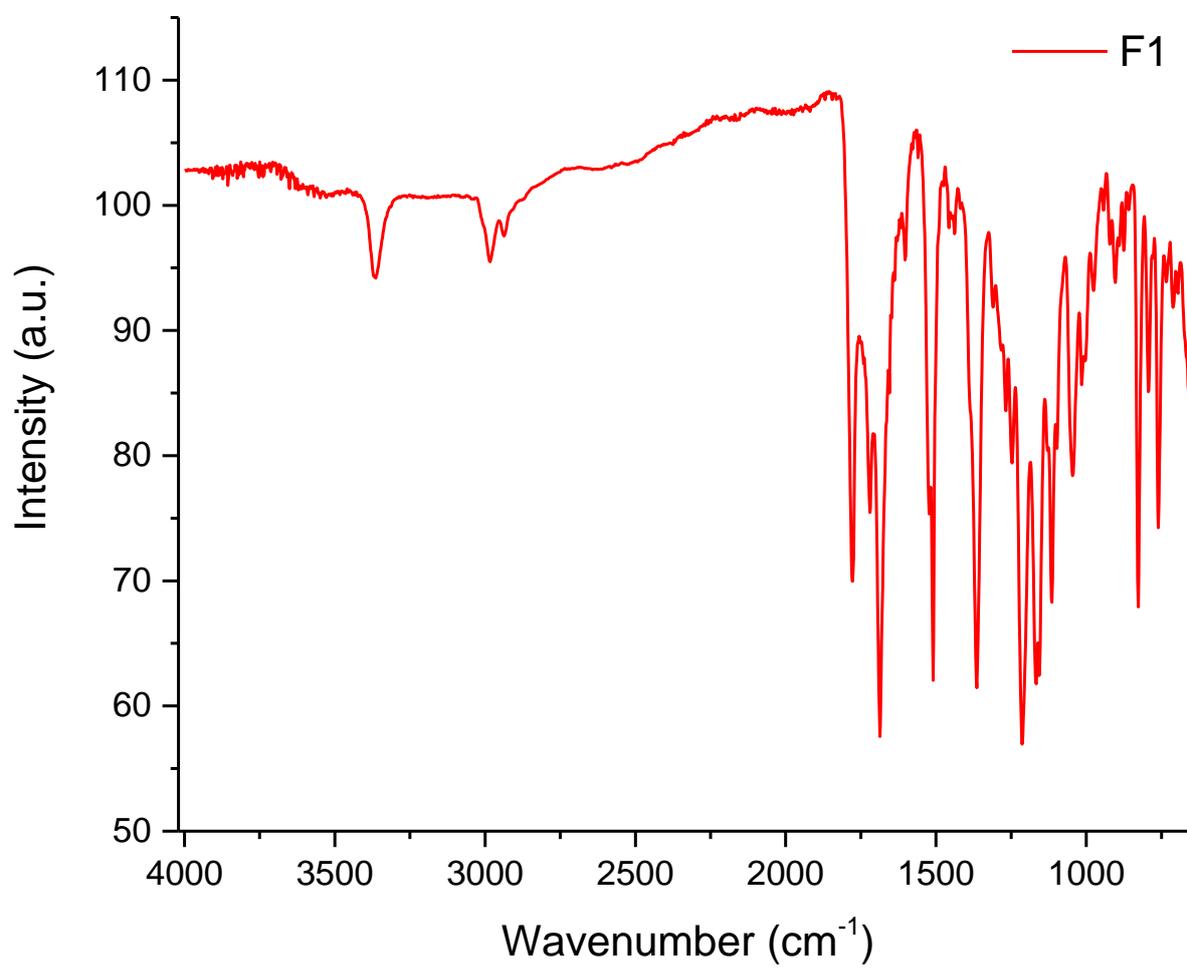


Table S1. Detailed list of the samples prepared with the solvent switch method

Entry	Conc.	Gelator	Solvent	Trigger	Outcome	Recovery
1	0.5%	F0	EtOH (30%)	Water (70%)	G	G
2	0.5%	F0	EtOH (50%)	Water (50%)	S	/
3	0.5%	F0	EtOH (70%)	Water (30%)	S	/
4	0.5%	F1	EtOH (30%)	Water (70%)	G	G
5	0.5%	F1	EtOH (50%)	Water (50%)	S	/
6	0.5%	F1	EtOH (70%)	Water (30%)	S	/
7	0.5%	F2	EtOH (30%)	Water (70%)	G	G
8	0.5%	F2	EtOH (50%)	Water (50%)	S	/
9	0.5%	F2	EtOH (70%)	Water (30%)	S	/
10	0.5%	F0	iPrOH (30%)	Water (70%)	S	/
11	0.5%	F0	iPrOH (50%)	Water (50%)	S	/
12	0.5%	F0	iPrOH (70%)	Water (30%)	S	/
13	0.5%	F1	iPrOH (30%)	Water (70%)	G	VS
14	0.5%	F1	iPrOH (50%)	Water (50%)	S	/
15	0.5%	F1	iPrOH (70%)	Water (30%)	S	/
16	0.5%	F2	iPrOH (30%)	Water (70%)	G	VS
17	0.5%	F2	iPrOH (50%)	Water (50%)	S	/
18	0.5%	F2	iPrOH (70%)	Water (30%)	S	/
19	1.0%	F0	EtOH (30%)	Water (70%)	G	G
20	1.0%	F0	EtOH (50%)	Water (50%)	S	/
21	1.0%	F0	EtOH (70%)	Water (30%)	S	/
22	1.0%	F1	EtOH (30%)	Water (70%)	G	G
23	1.0%	F1	EtOH (50%)	Water (50%)	S	/
24	1.0%	F1	EtOH (70%)	Water (30%)	S	/
25	1.0%	F2	EtOH (30%)	Water (70%)	G	G
26	1.0%	F2	EtOH (50%)	Water (50%)	S	/
27	1.0%	F2	EtOH (70%)	Water (30%)	S	/
28	1.0%	F0	iPrOH (30%)	Water (70%)	G	G
29	1.0%	F0	iPrOH (50%)	Water (50%)	S	/
30	1.0%	F0	iPrOH (70%)	Water (30%)	S	/
31	1.0%	F1	iPrOH (30%)	Water (70%)	G	G
32	1.0%	F1	iPrOH (50%)	Water (50%)	P	/
33	1.0%	F1	iPrOH (70%)	Water (30%)	S	/
34	1.0%	F2	iPrOH (30%)	Water (70%)	G	G
35	1.0%	F2	iPrOH (50%)	Water (50%)	S	/
36	1.0%	F2	iPrOH (70%)	Water (30%)	S	/

G = gel; S = solution; VS = viscous solution; P = precipitate

Table S2. Detailed list of the samples prepared with the pH change method and the addition of calcium chloride

Entry	Methodology	Conc.	Gelator	Solvent ^a	Trigger (eq)	Outcome	pH	Recovery
37	b	0.5%	F0	0.03 M PBS	GdL (1.4)	G	3.8	G
38	b	0.5%	F1	0.03 M PBS	GdL (1.4)	G	3.9	G
39	b	0.5%	F2	0.03 M PBS	GdL (1.4)	G	4.2	G
40	c	0.5%	F0	0.03 M PBS	CaCl ₂ (1.0)	PG	/	/
41	c	0.5%	F1	0.03 M PBS	CaCl ₂ (1.0)	G	4.4	PG
42	c	0.5%	F2	0.03 M PBS	CaCl ₂ (1.0)	G	4.6	PG
43	b	1.0%	F0	0.06 M PBS	GdL (1.4)	G	3.6	G
44	b	1.0%	F1	0.06 M PBS	GdL (1.4)	G	3.7	G
45	b	1.0%	F2	0.06 M PBS	GdL (1.4)	G	3.8	G
46	c	1.0%	F0	0.06 M PBS	CaCl ₂ (1.0)	G	4.5	G
47	c	1.0%	F1	0.06 M PBS	CaCl ₂ (1.0)	G	4.7	G
48	c	1.0%	F2	0.06 M PBS	CaCl ₂ (1.0)	G	4.8	G

^a Final concentration; G = gel; PG = partial gel

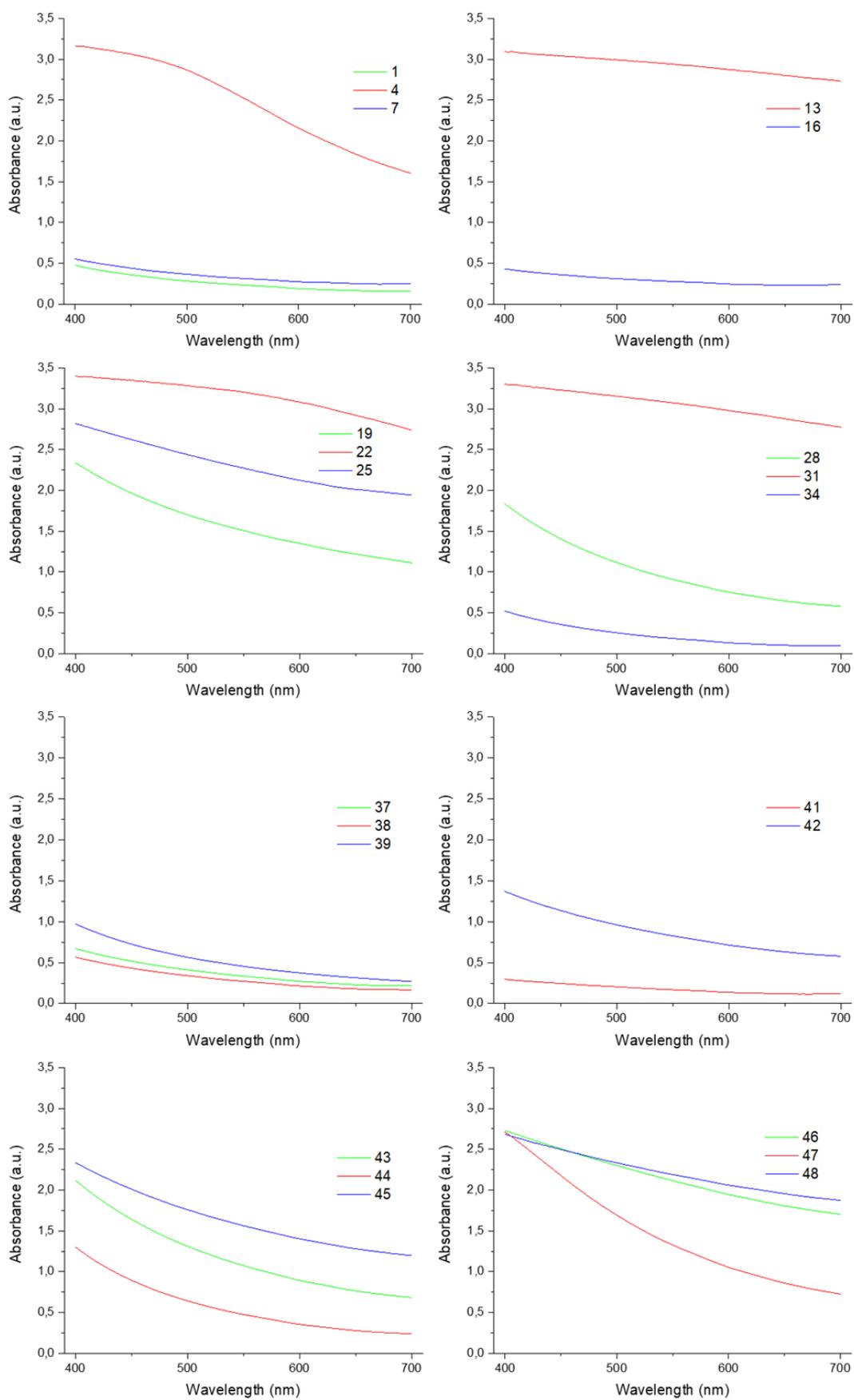


Figure S1. Absorbance spectra of the gels samples.

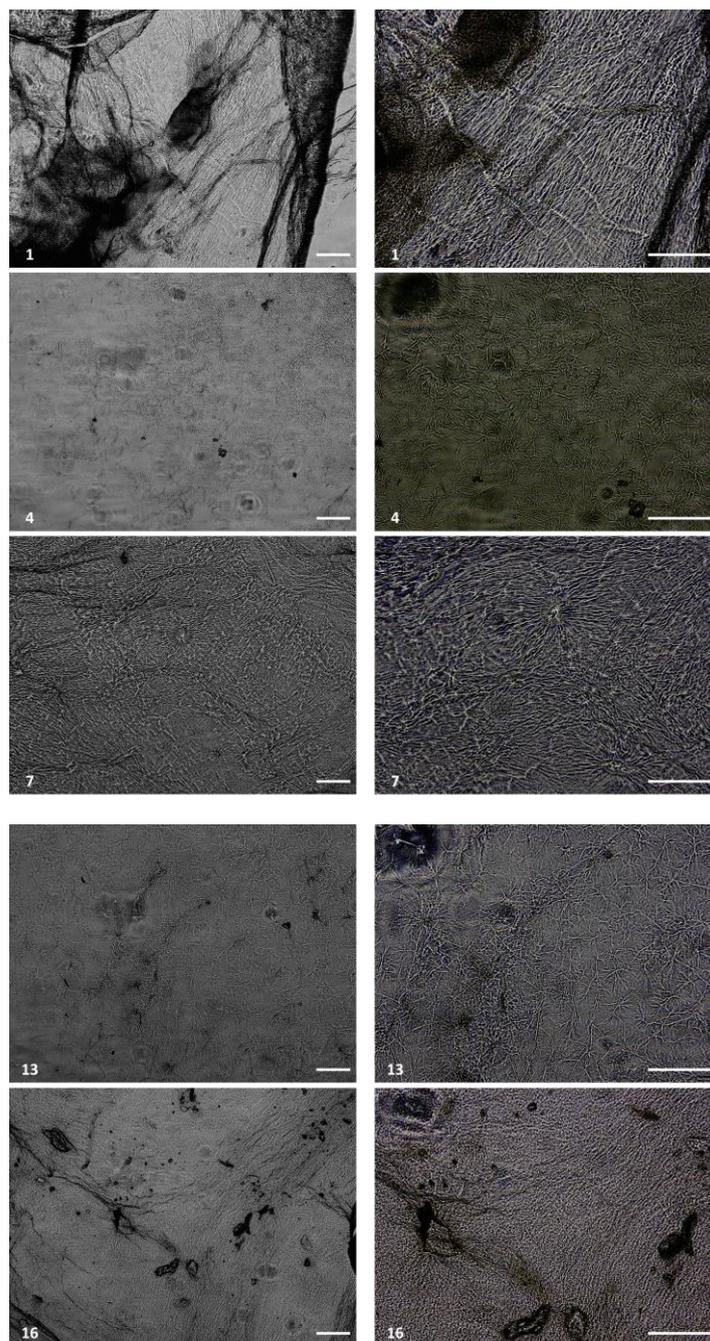


Figure S2. Morphology of the dried hydrogels **1, 4, 7, 13** and **16**, analysed through an optical microscope with different magnifications. Left: 10x magnification. Right: 20x magnification. For all the images the scalebar is 100 μm .

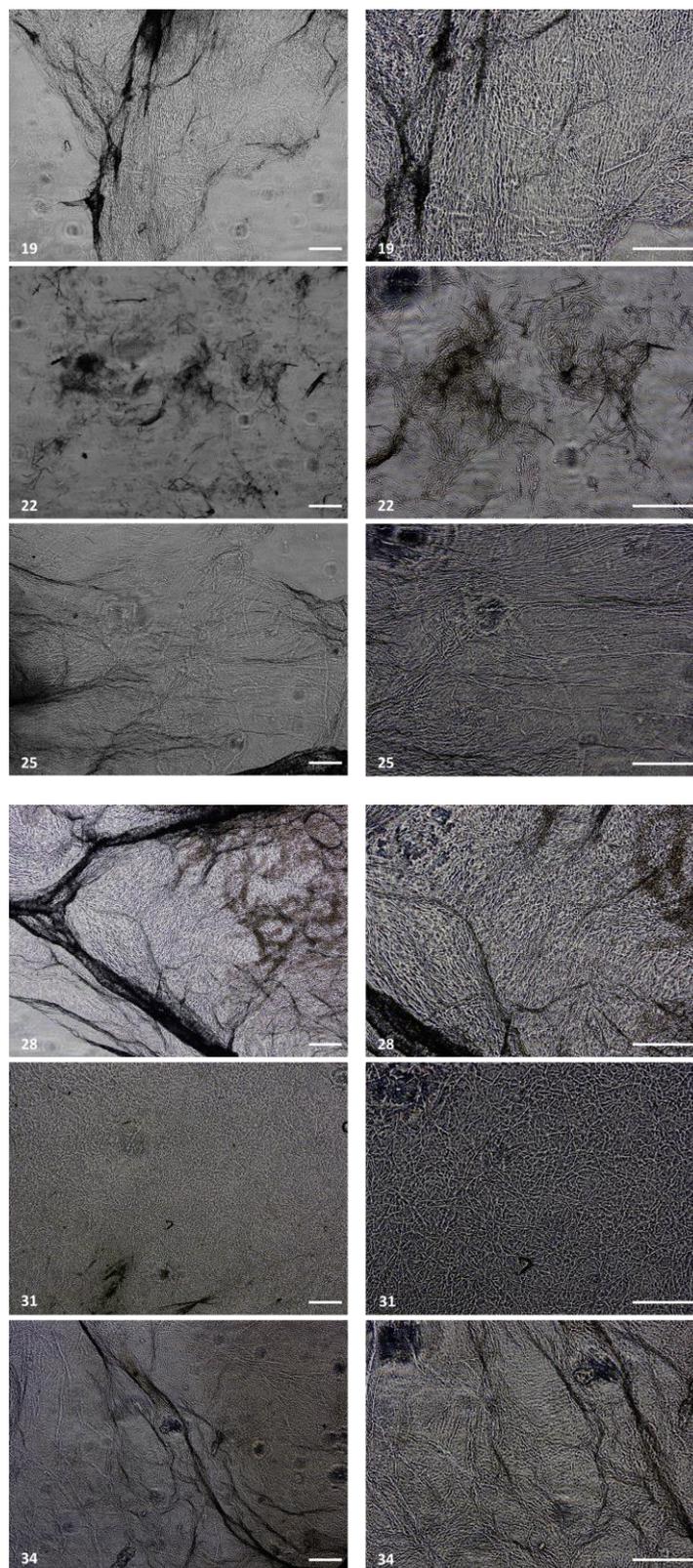


Figure S3. Morphology of the dried hydrogels 19, 22, 25, 28, 31 and 34, analysed through an optical microscope with different magnifications. Left: 10x magnification. Right: 20x magnification. For all the images the scalebar is 100 μm .

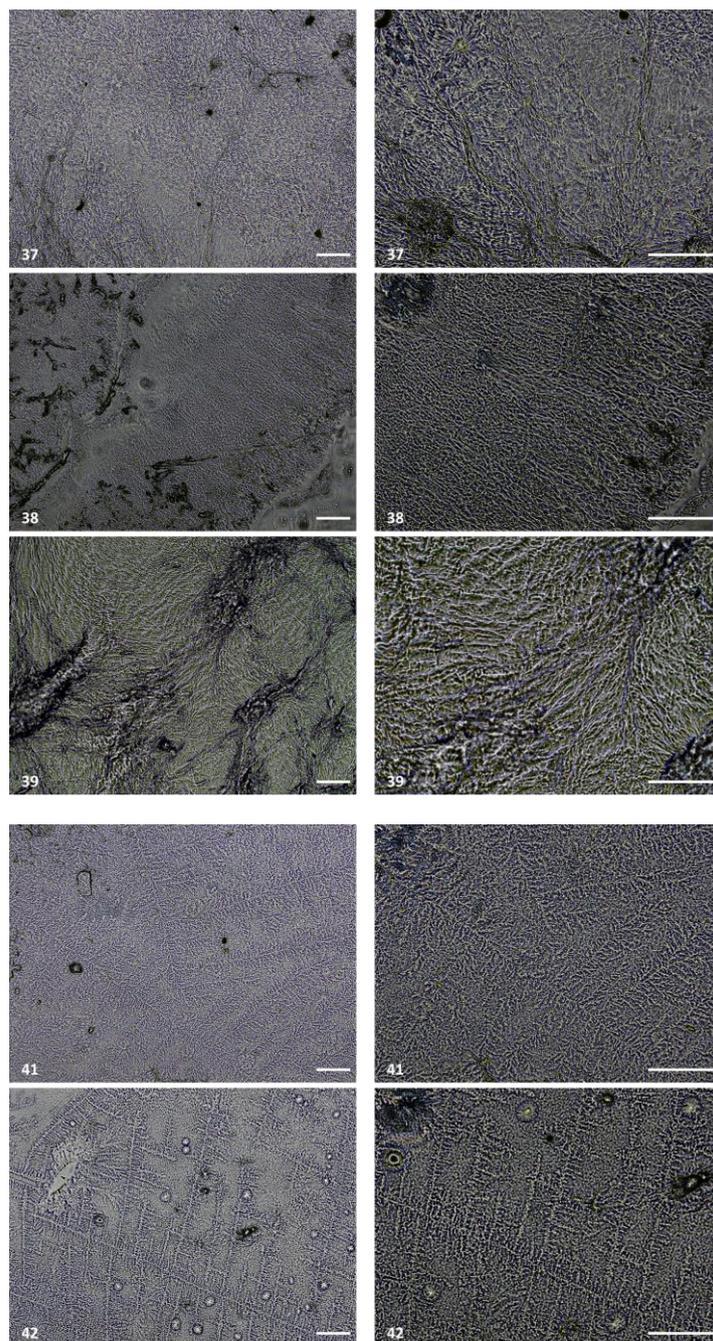


Figure S4. Morphology of the dried hydrogels 37, 38, 39, 41 and 42, analysed through an optical microscope with different magnifications. Left: 10x magnification. Right: 20x magnification. For all the images the scalebar is 100 μm .

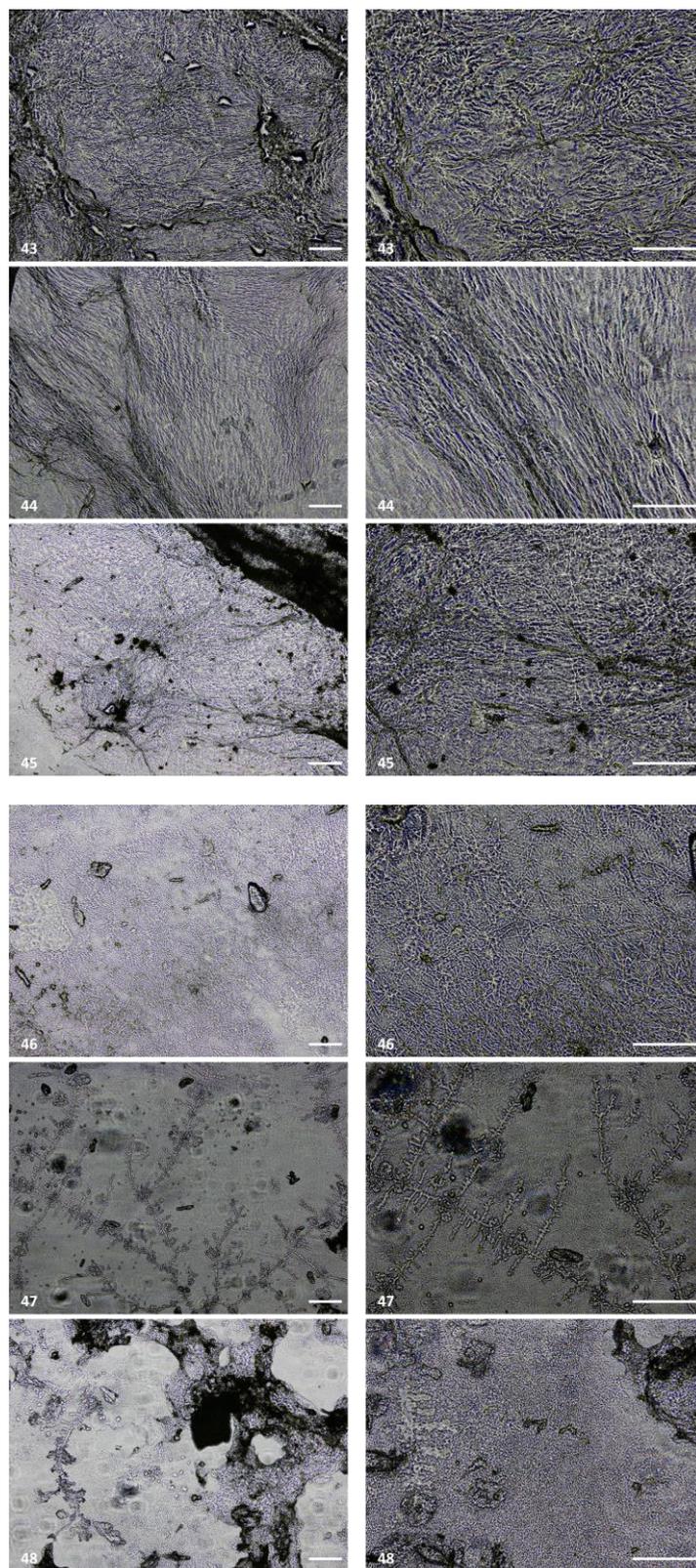


Figure S5. Morphology of the dried hydrogels **43**, **44**, **45**, **46**, **47** and **48**, analysed through an optical microscope with different magnifications. Left: 10x magnification. Right: 20x magnification. For all the images the scalebar is 100 μm .

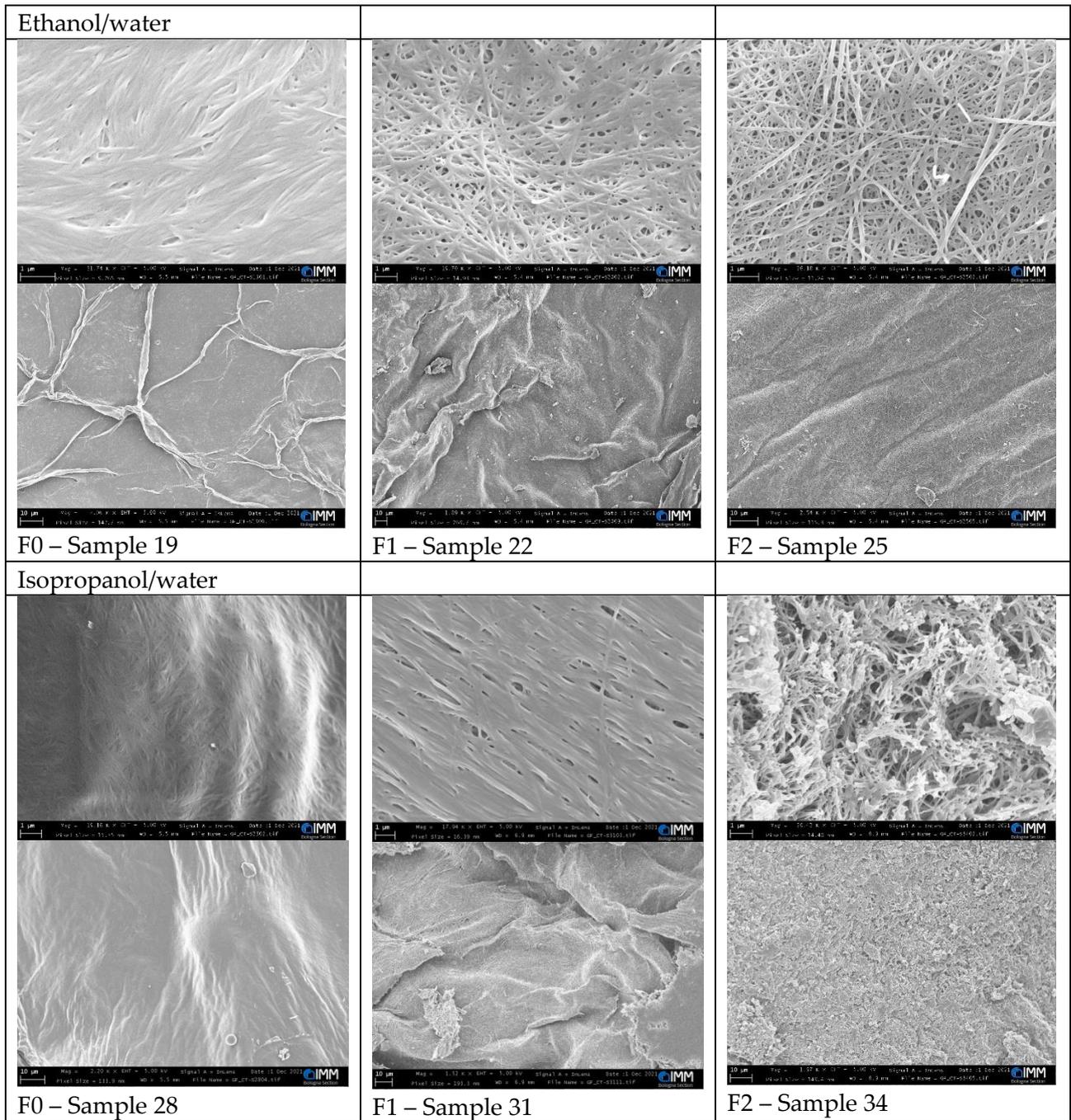


Figure S6. SEM images of the dried hydrogels 19, 22, 25, 28, 31 and 34.

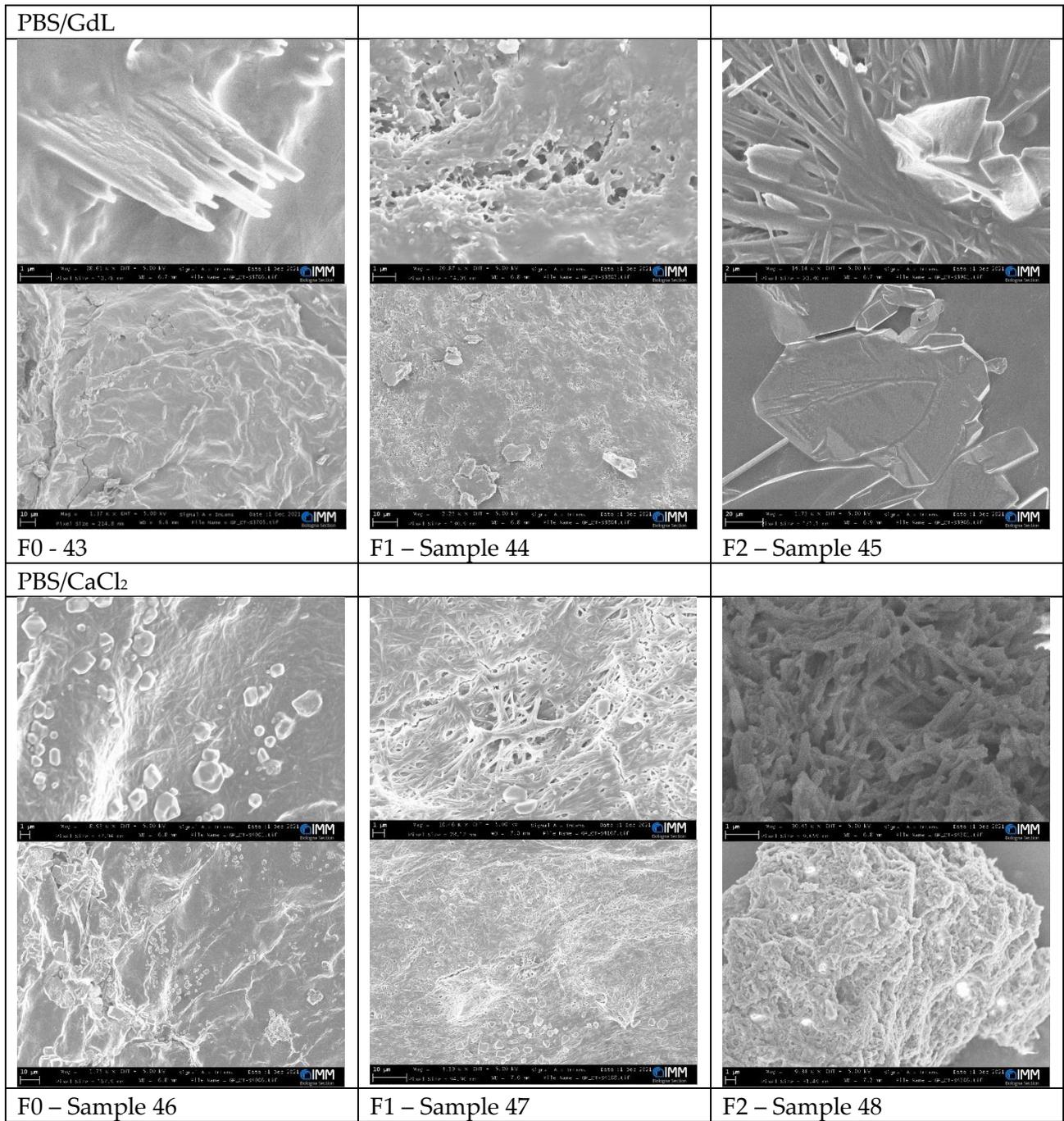


Figure S7. SEM images of the dried hydrogels 43-48.

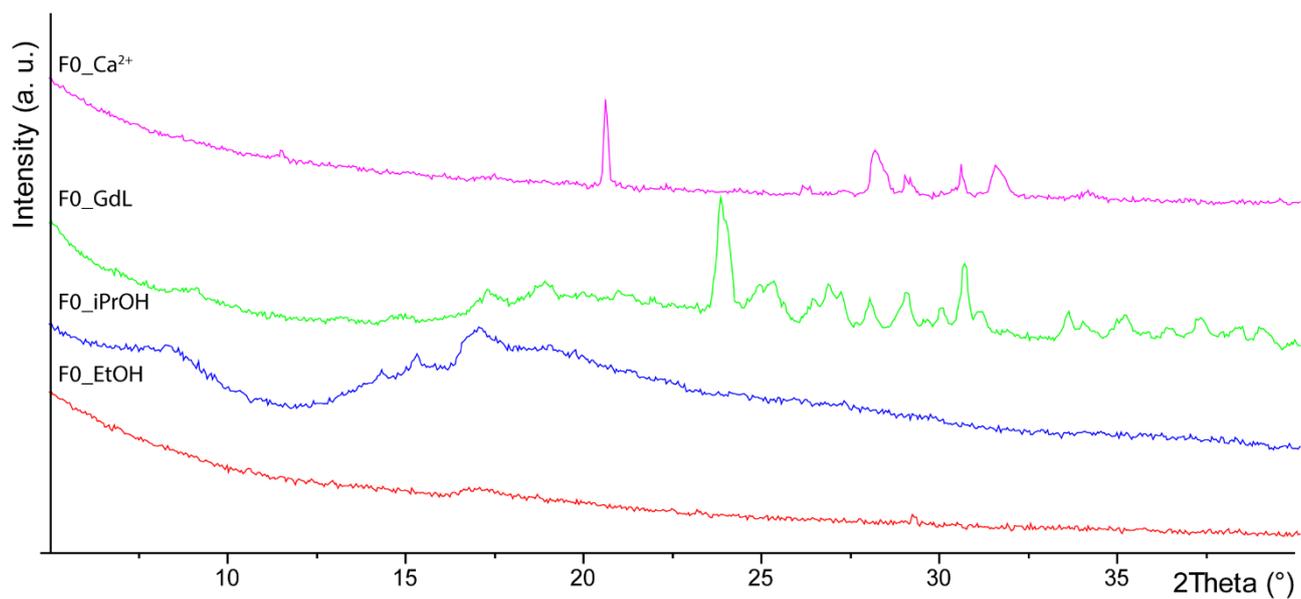


Figure S8. X-ray powder diffraction patterns of the xerogels from molecules F0 obtained from different chemical systems. F0_EtOH, F0_iPrOH, F0_GdL, and F0_Ca²⁺ correspond to 19, 28, 37 and 40, respectively.

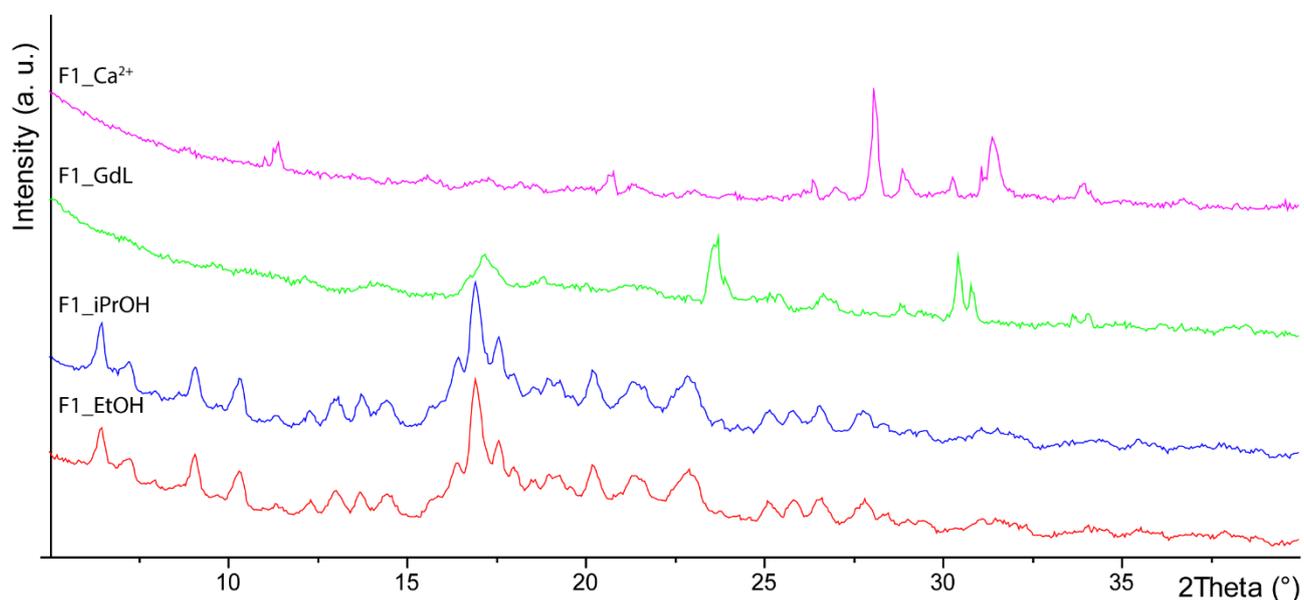


Figure S9. X-ray powder diffraction patterns of the xerogels from molecules F0 obtained from different chemical systems. F1_EtOH, F1_iPrOH, F1_GdL, and F1_Ca²⁺ correspond to 22, 31, 38 and 41, respectively.

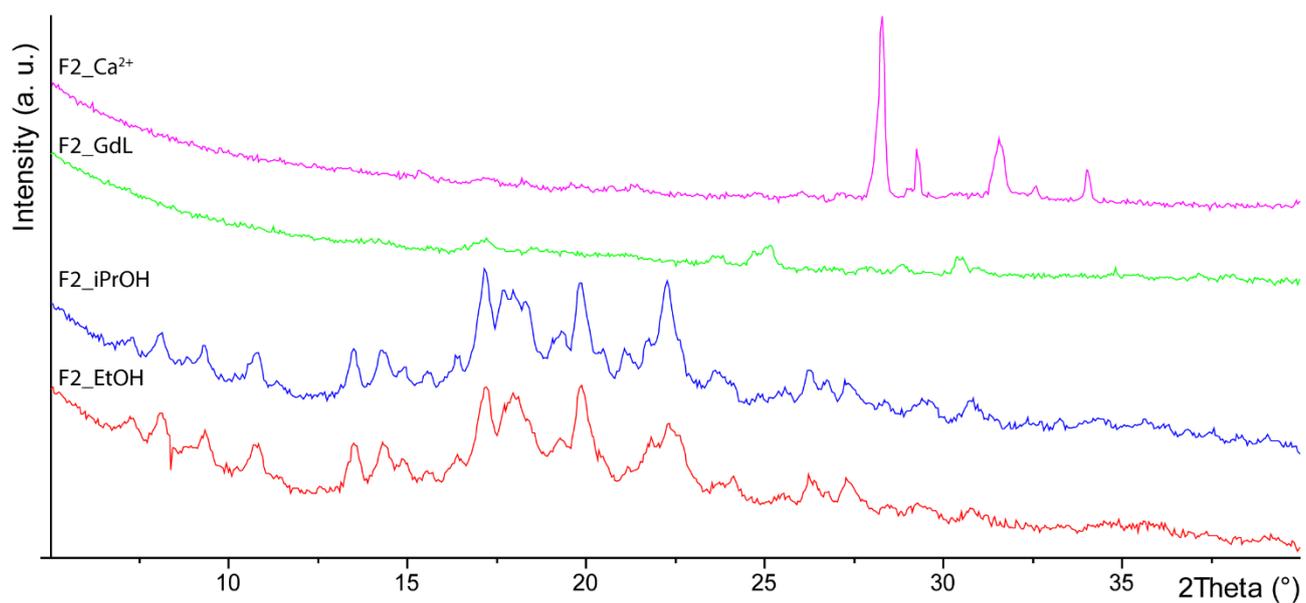


Figure S10. X-ray powder diffraction patterns of the xerogels from molecules F0 obtained from different chemical systems. F2_EtOH, F2_iPrOH, F2_GdL, and F2_Ca²⁺ correspond to 25, 34, 39 and 42, respectively.

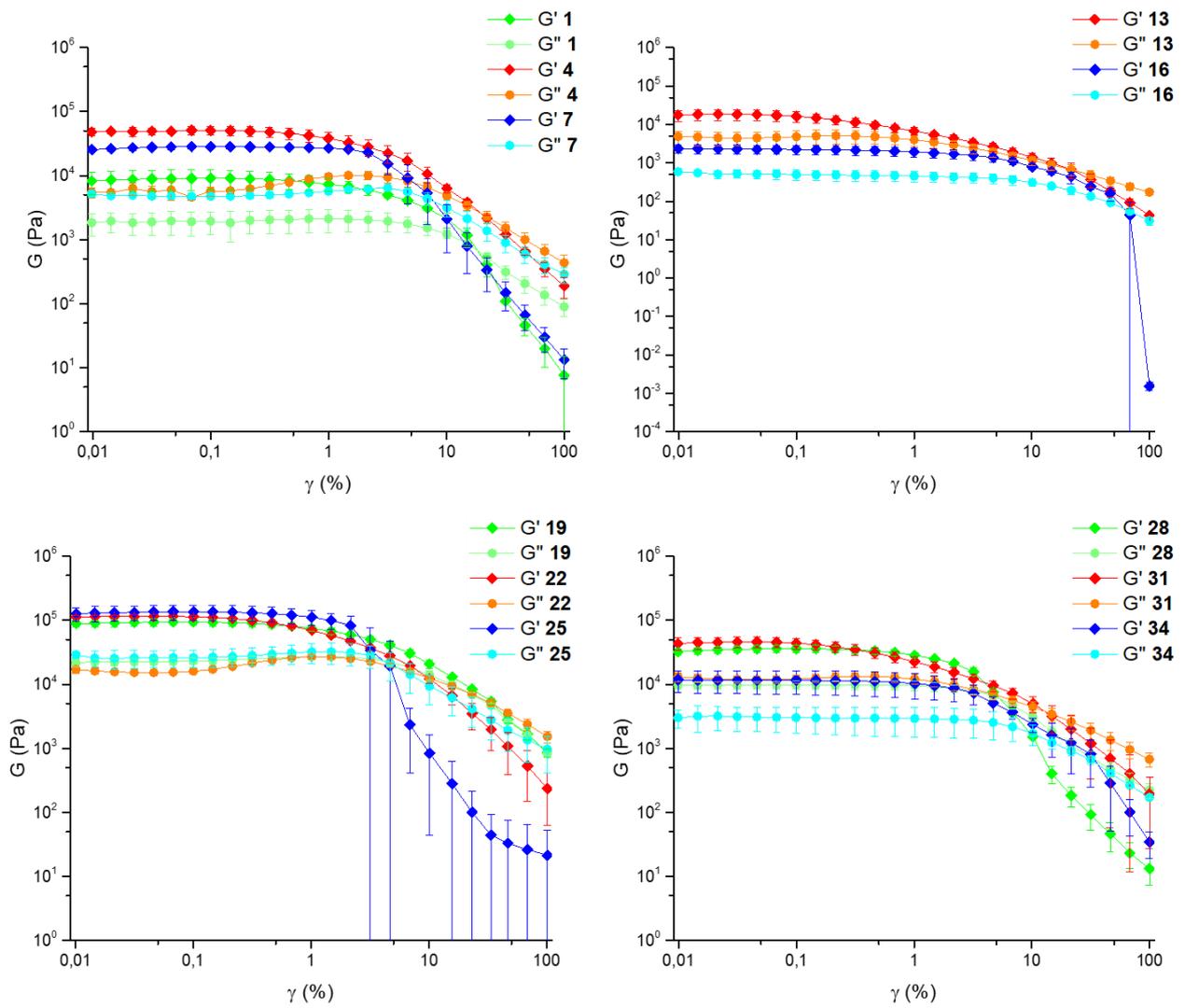


Figure S11. Amplitude sweep analysis of the samples 1, 4, 7, 13, 16, 19, 22, 25, 28, 31 and 34.

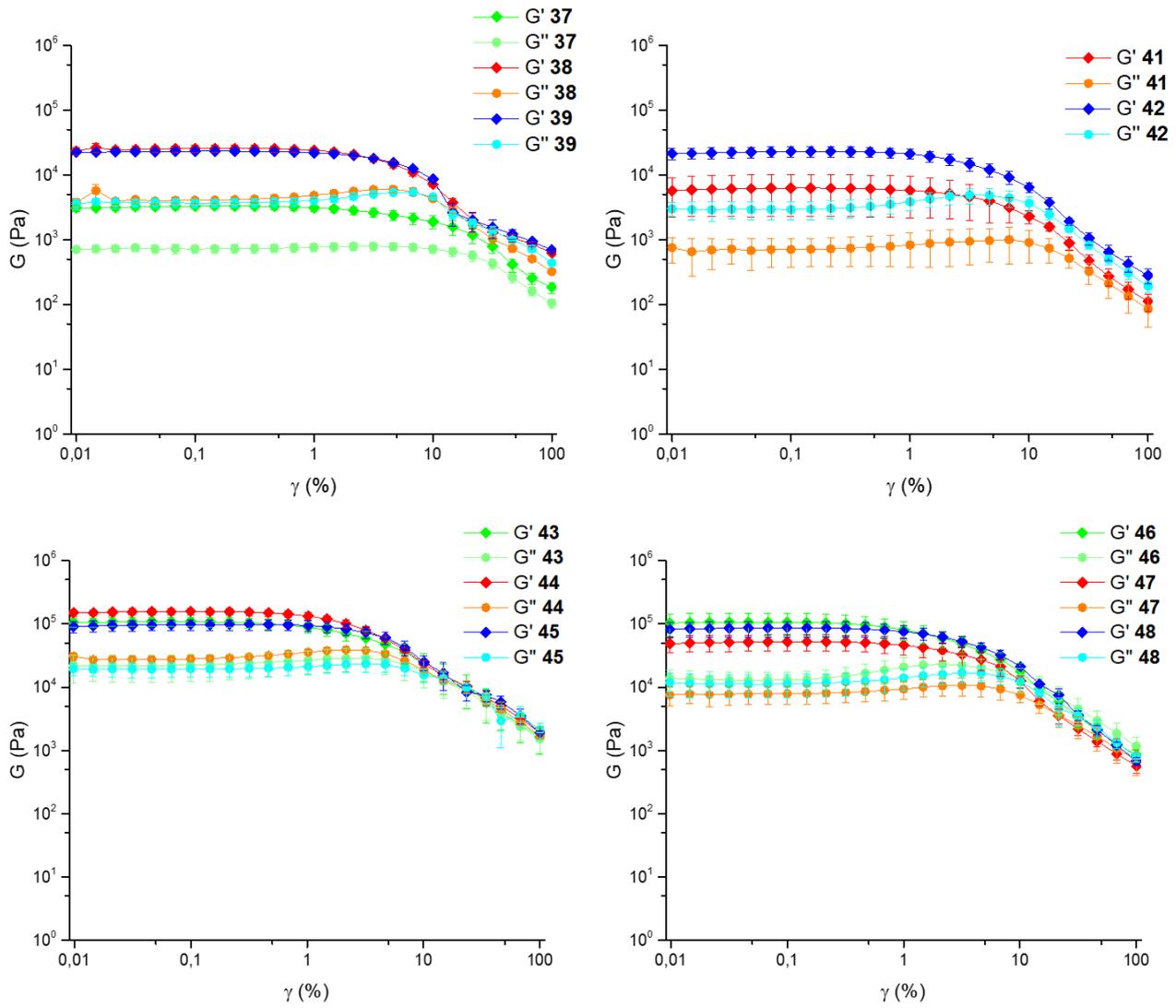


Figure S12. Amplitude sweep analysis of the samples 37, 38, 39 and 41-48.

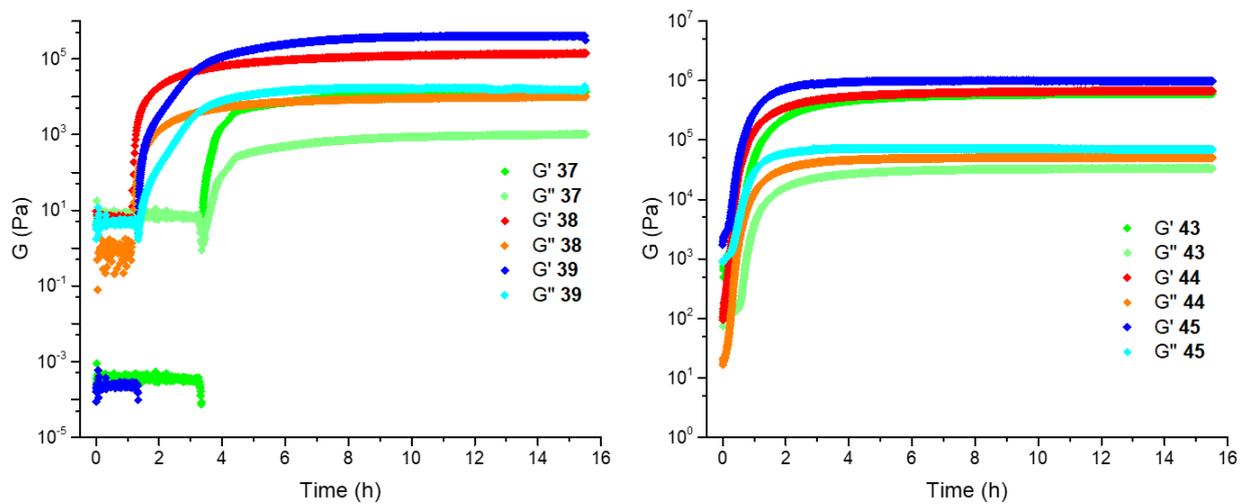


Figure S13. Time sweep analysis of the samples 37-39 and 43-45 obtained with the addition of GdL.

Table S3. Summary of the Properties of Gels

Sample	Gelator	Conc.	Recovery	pH	A ($\lambda=630$ nm)	T (%)	G' (kPa) ($\gamma = 0.068\%$)	G'' (kPa) ($\gamma = 0.068\%$)
EtOH/H ₂ O								
1	F0	0.5	yes	n.a.	0.17469	66.88	9.06 ± 3.27	1.91 ± 0.77
4	F1	0.5	yes	n.a.	1.96473	1.08	51.18 ± 8.04	4.59 ± 0.54
7	F2	0.5	yes	n.a.	0.26185	54.72	28.29 ± 2.47	4.74 ± 0.32
19	F0	1.0	yes	n.a.	1.26706	5.41	93.79 ± 11.23	22.80 ± 2.73
22	F1	1.0	yes	n.a.	2.98876	0.10	114.96 ± 6.24	15.44 ± 1.17
25	F2	1.0	yes	n.a.	2.04926	0.89	135.93 ± 35.36	25.94 ± 7.91
iPrOH/H ₂ O								
13	F1	0.5	no	n.a.	2.83436	0.15	17.26 ± 5.43	4.57 ± 1.79
16	F2	0.5	no	n.a.	0.23566	58.12	2.25 ± 0.58	0.51 ± 0.15
28	F0	1.0	yes	n.a.	0.68608	20.60	36.07 ± 4.62	9.74 ± 1.36
31	F1	1.0	yes	n.a.	2.92284	0.12	45.29 ± 8.55	11.93 ± 1.71
34	F2	1.0	yes	n.a.	0.11273	77.14	11.61 ± 4.58	3.06 ± 1.30
PBS/GdL								
37	F0	0.5	yes	3.8	0.24547	56.82	3.29 ± 0.35	0.73 ± 0.12
38	F1	0.5	yes	3.9	0.19197	64.27	25.39 ± 3.00	4.06 ± 0.42
39	F2	0.5	yes	4.2	0.33574	46.16	23.15 ± 1.31	3.73 ± 0.57
43	F0	1.0	yes	3.6	0.8128	15.39	109.16 ± 18.09	22.21 ± 10.22
44	F1	1.0	yes	3.7	0.30614	49.41	157.02 ± 18.62	27.78 ± 2.03
45	F2	1.0	yes	3.8	1.32719	4.71	97.00 ± 18.39	19.30 ± 5.16
PBS/Ca ²⁺								
41	F1	0.5	no	4.4	0.12512	74.97	6.23 ± 3.93	0.71 ± 0.33
42	F2	0.5	no	4.6	0.66275	21.74	22.85 ± 4.27	2.94 ± 0.91
46	F0	1.0	yes	4.5	1.86026	1.38	106.98 ± 41.32	12.90 ± 4.31
47	F1	1.0	yes	4.7	0.93284	11.67	52.18 ± 14.65	7.83 ± 2.54
48	F2	1.0	yes	4.8	1.99850	1.00	86.82 ± 23.94	11.13 ± 4.39

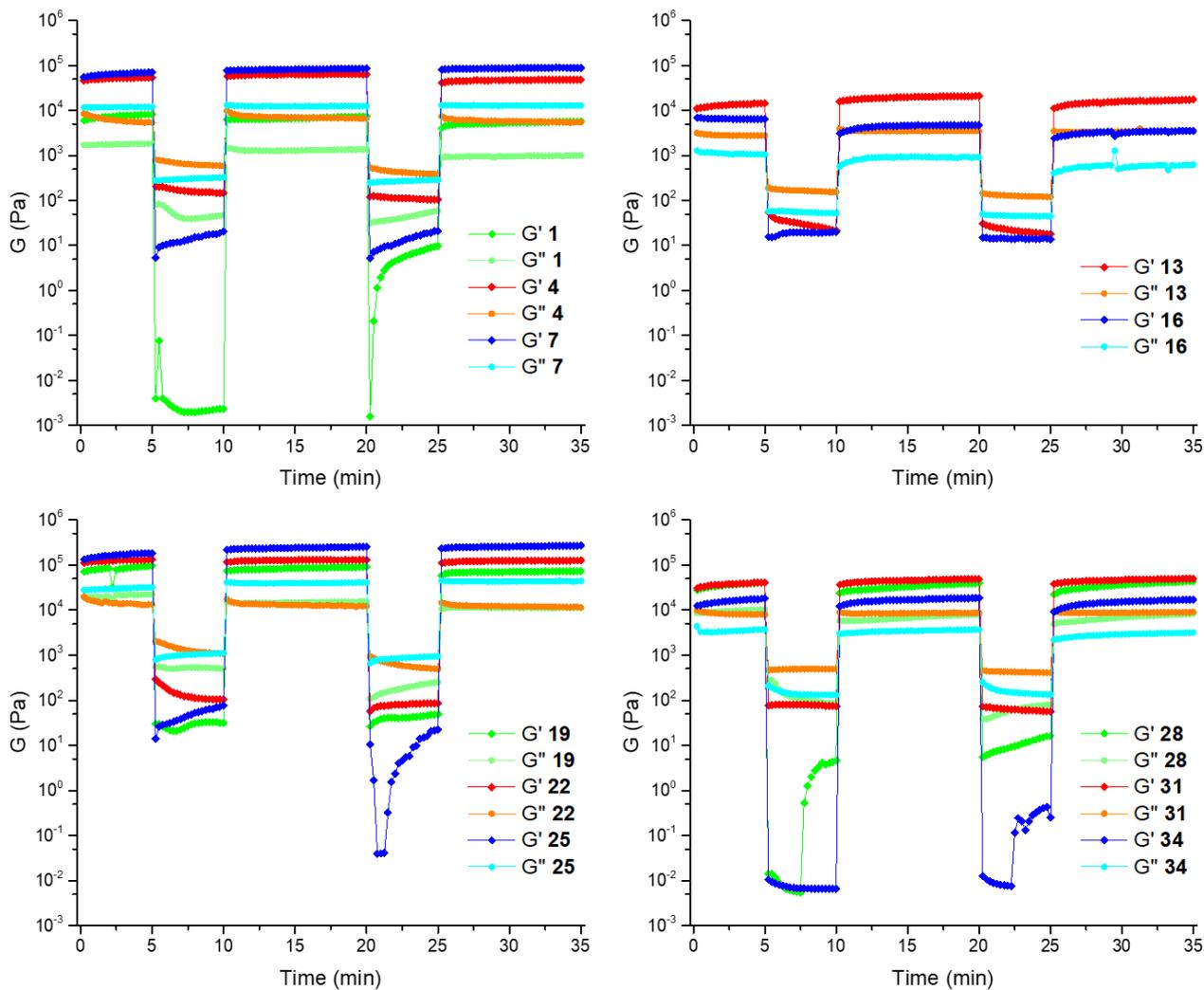


Figure S14. Thixotropic behaviour of the samples 1, 4, 7, 13, 16, 19, 22, 25, 28, 31 and 34 analysed with the rheometer.

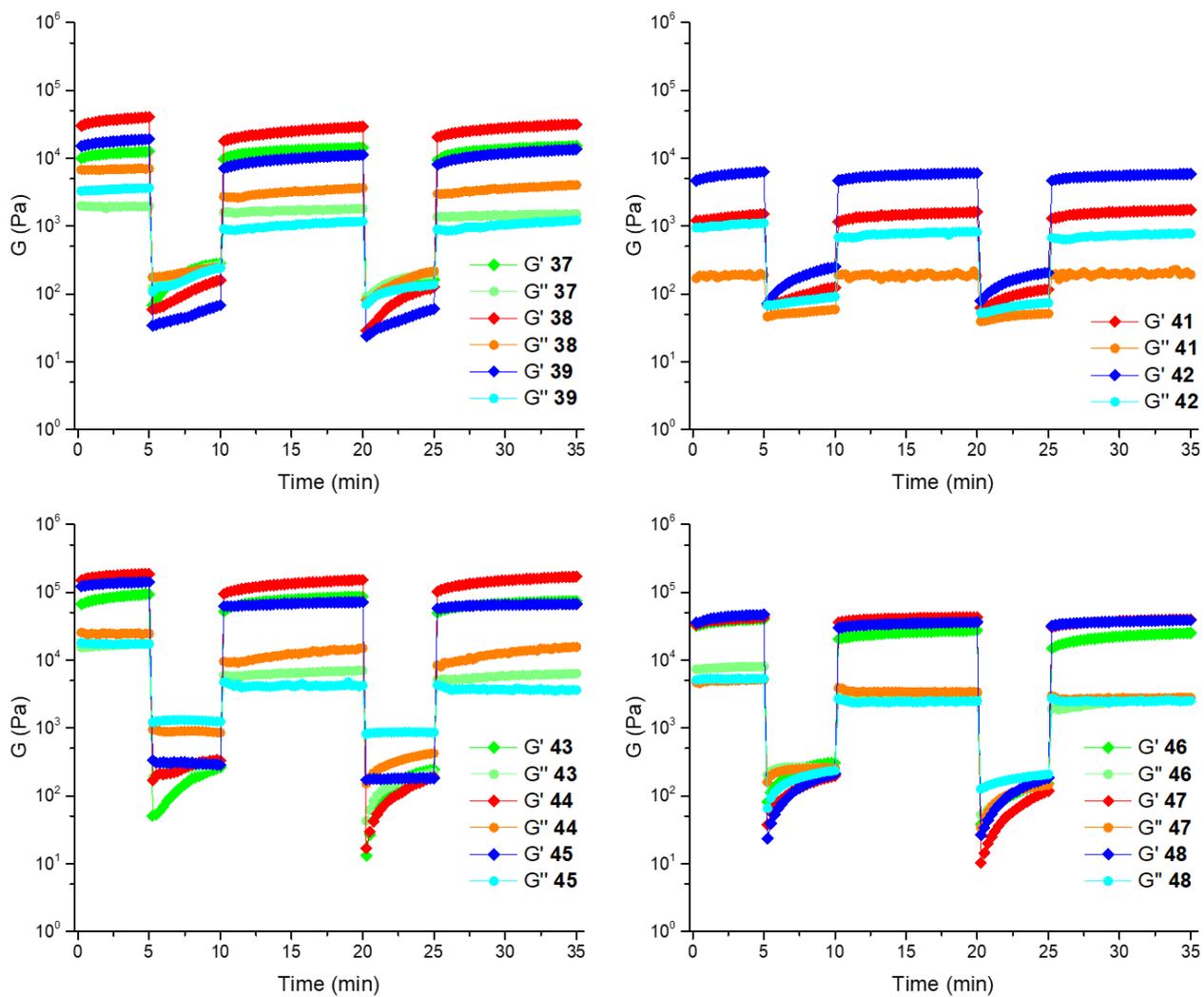


Figure S15. Thixotropic behaviour of the samples 37, 38, 39 and 41-48, analysed with the rheometer.

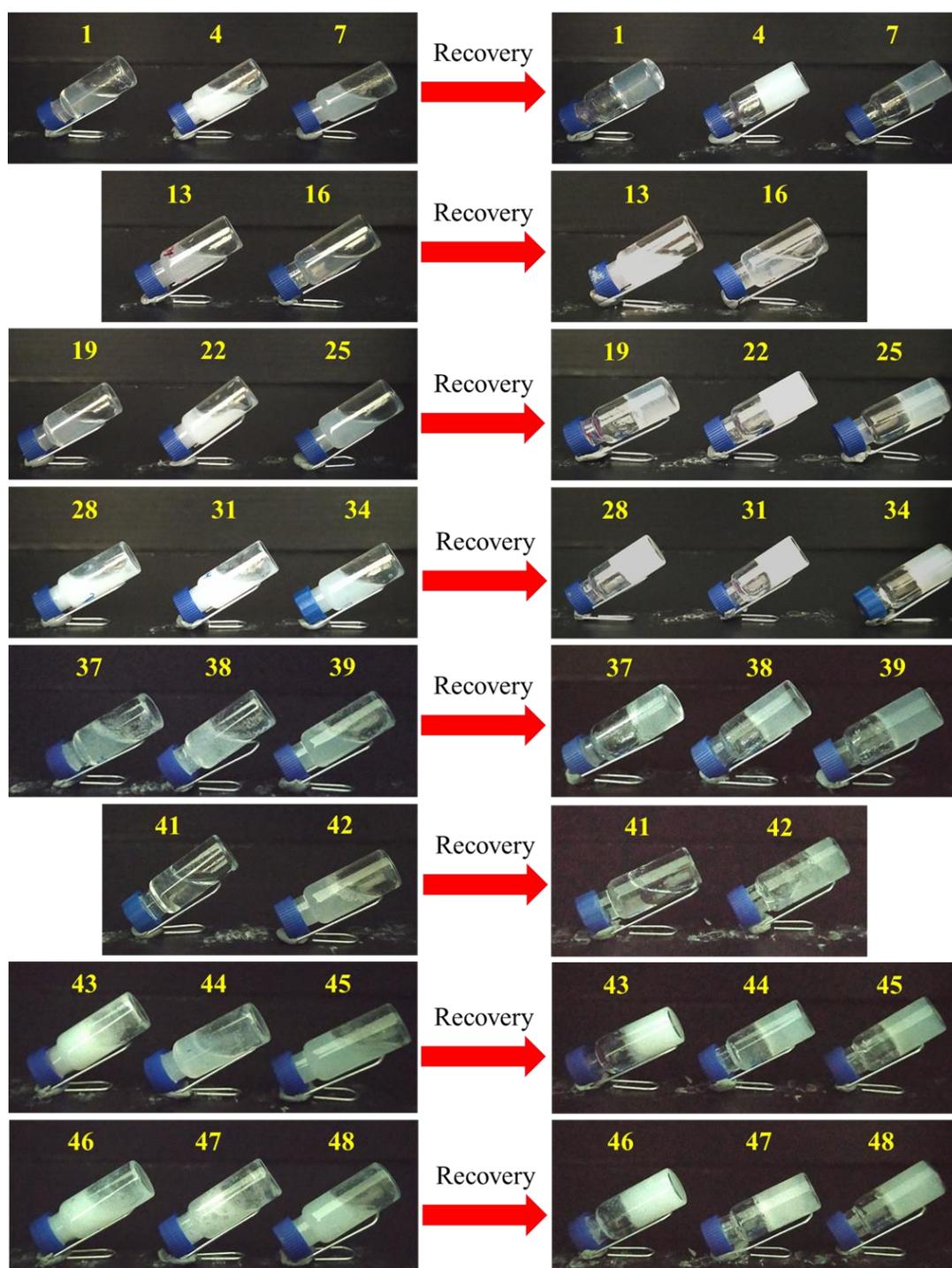


Figure S16. Thixotropic behaviour of the gels formed after vigorous shaking (left) and 16 hours of recovery (right).

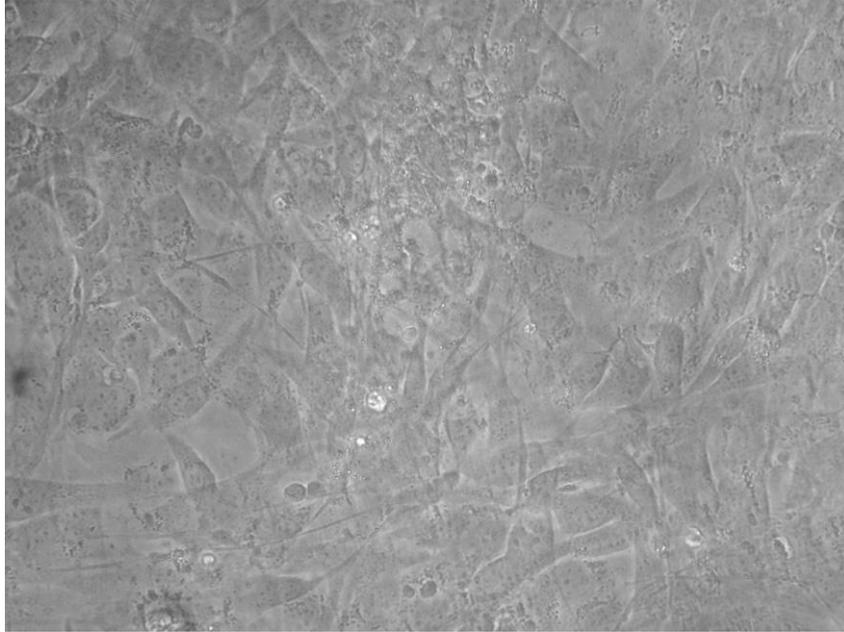


Figure S17. Optical micrograph of cells in DPBS (control).