Supporting Information

Coaxial mussel-inspired biofibers: Making of a robust and efficacious depot for cancer drug delivery

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Analysis of dye loaded fibers

Degree of substitution of alginate-dopamine was shown to have a significant effect on the dye release profile and total amount of dye released. Accordingly, fibers made from alginate-dopamine 50% had the slowest release (51 μgr), followed by the fibers made from alginate-dopamine 25% (32 μgr) and pure alginate (22 μgr), respectively (Figure S2, supporting information). Noting, these observations were likely due to strong intramolecular interactions of the dye and the catechol moeities in alginate-dopamine fibers.[1]

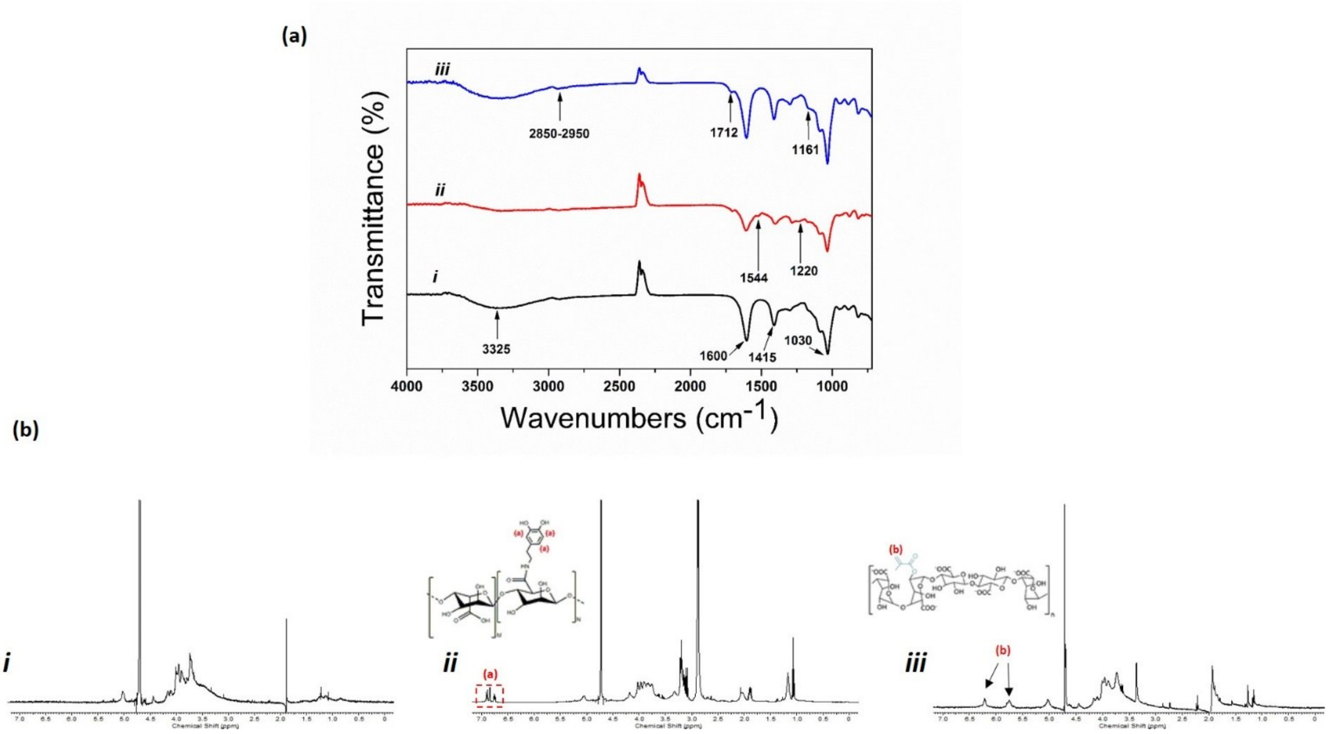

Figure S1. Physiochemical characterization of as-synthesized polymers including, **(a & b)** FTIR and HNMR spectra of i) pure alginate, ii) alginate-dopamione, and iii) alginate-methacrylate.

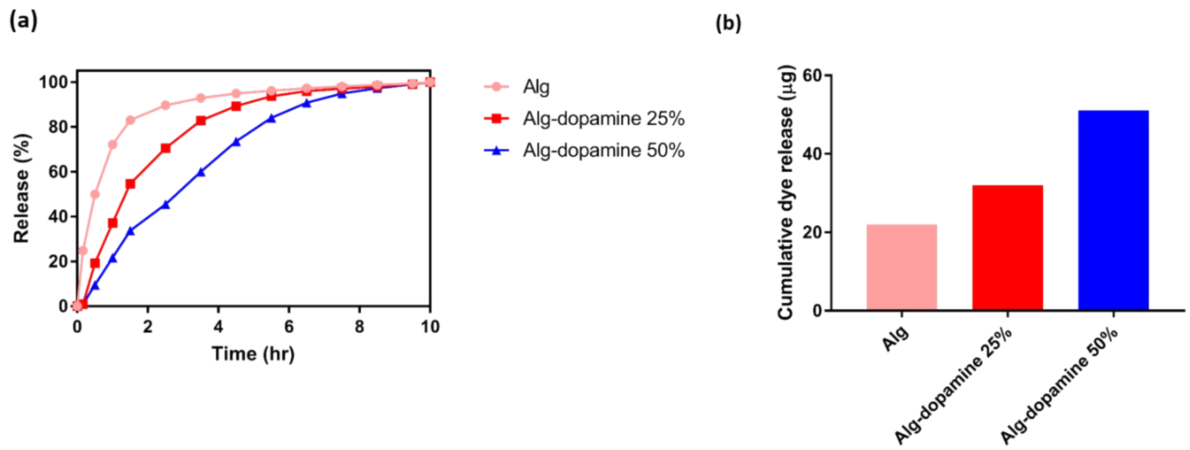

Figure S2. Preliminary dye release (fluorescein sodium salt, 2mM) studies from single fibers made from pure alginate (Alg), alginate-dopamine 25% (alg-dopamine 25%), alginate-dopamine 50% (Alg-dopamine 50%) **(a)** Release profile of dye loaded fibers. **(b)** Cumulative dye released from the fibers.

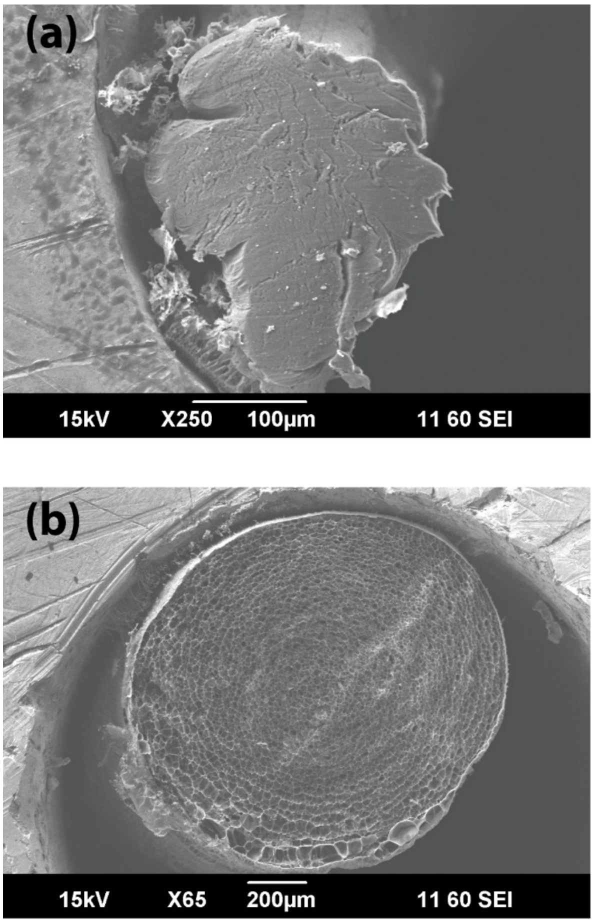

Figure S3. Morphology of single fibers made from pure alginate (Alg) using SEM imaging, **(a)** in dry state, **(b)** in complete swollen state after 2 hr of immersion in SBF.

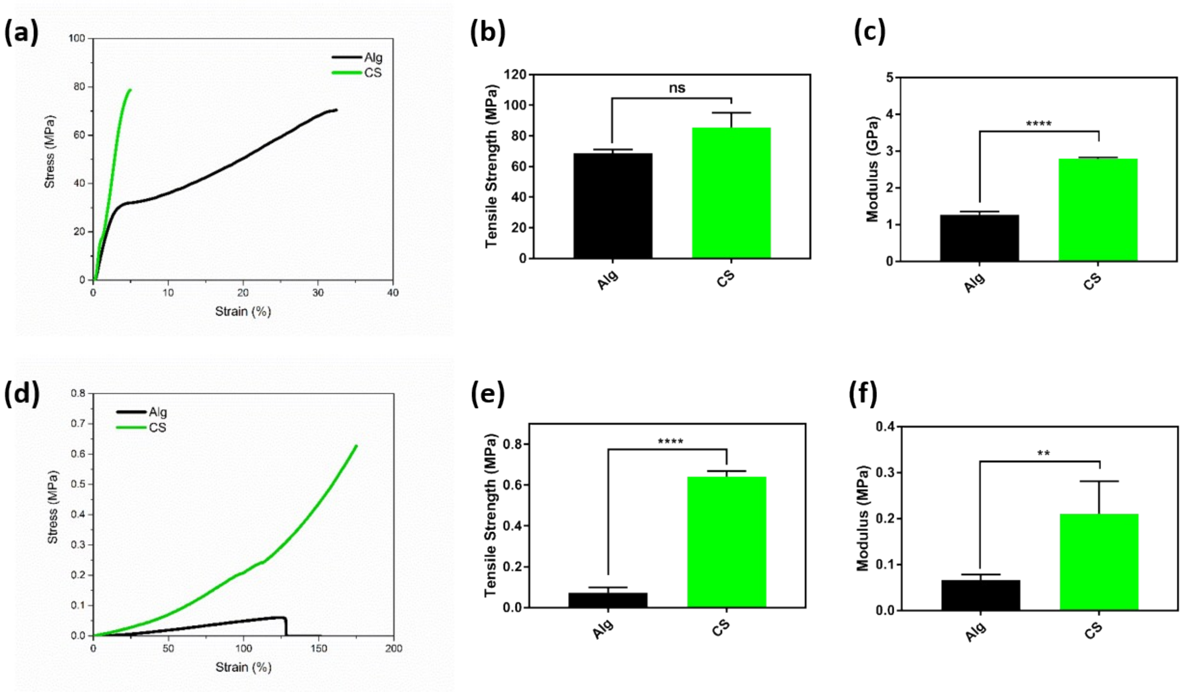

Figure S4. Mechanical properties of fibers following a static tensile test, pure alginate fibers (Alg) or core-shell mussel-inspired fibers (CS), **(a)** Stress-strain curve for fibers in dry state. **(b & c)** Tensile strength and modulus of fibers in dry state (n = 3, mean ± SD). **(d)** Stress-strain curve for fibers in wet state. **(e & f)** Tensile strength and modulus of fibers in wet state (n = 3, mean ± SD) (**P ≤ 0.01, ****P = 0.0001).

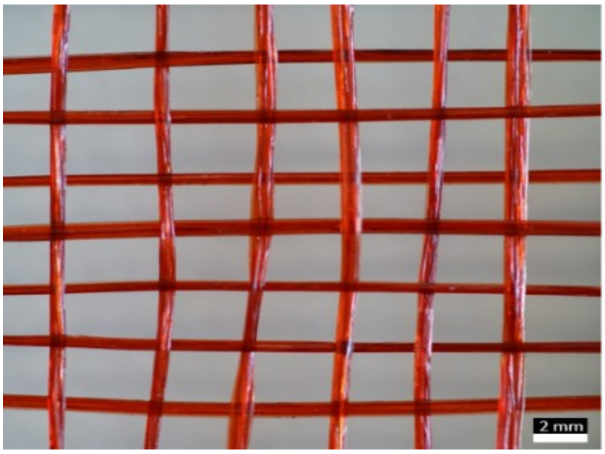

Figure S5. Microscopy image of woven DOX-loaded CS fibers (scale bar 2 mm).

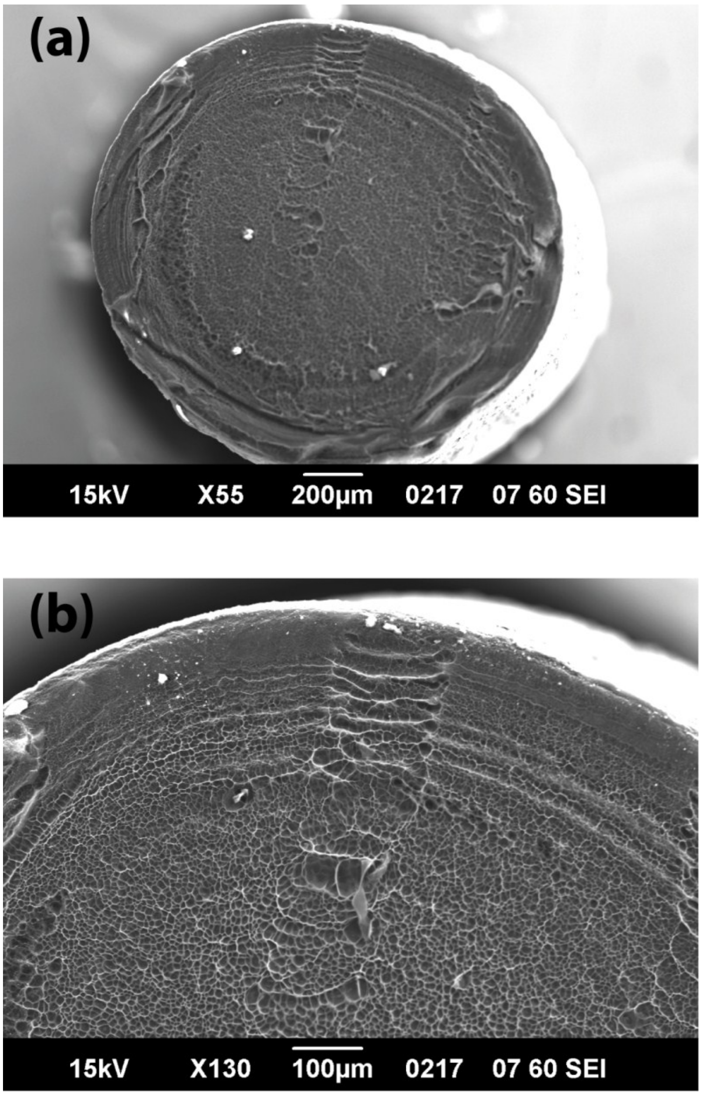

Figure S6. Morphology of wet CS• fibers where both core and shell were made from UV-crosslinkable alginate-methacrylate (3% w/v).

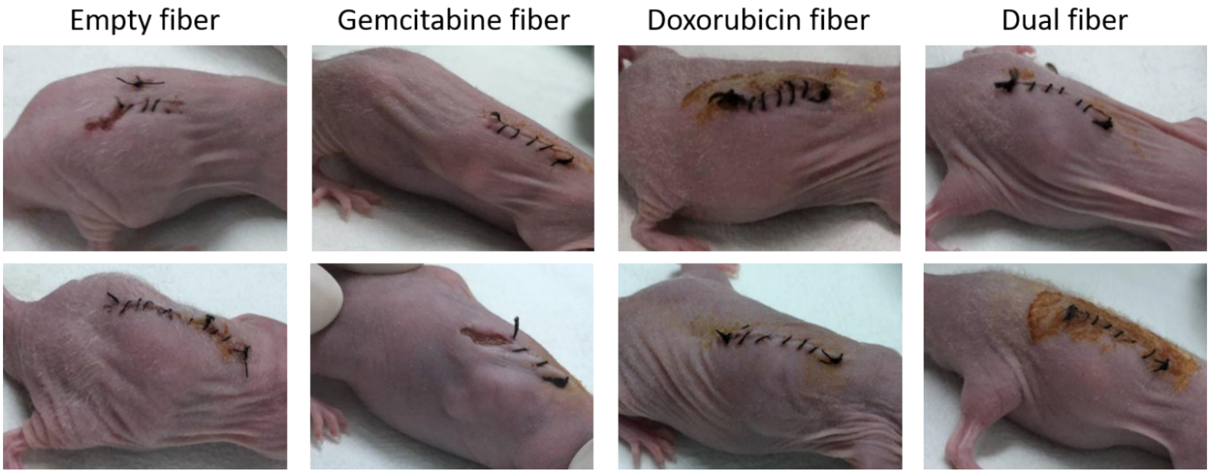

Figure S7. Images of tumor bearing mice (MIA PaCa-2) 2 days after implantation of fibers.

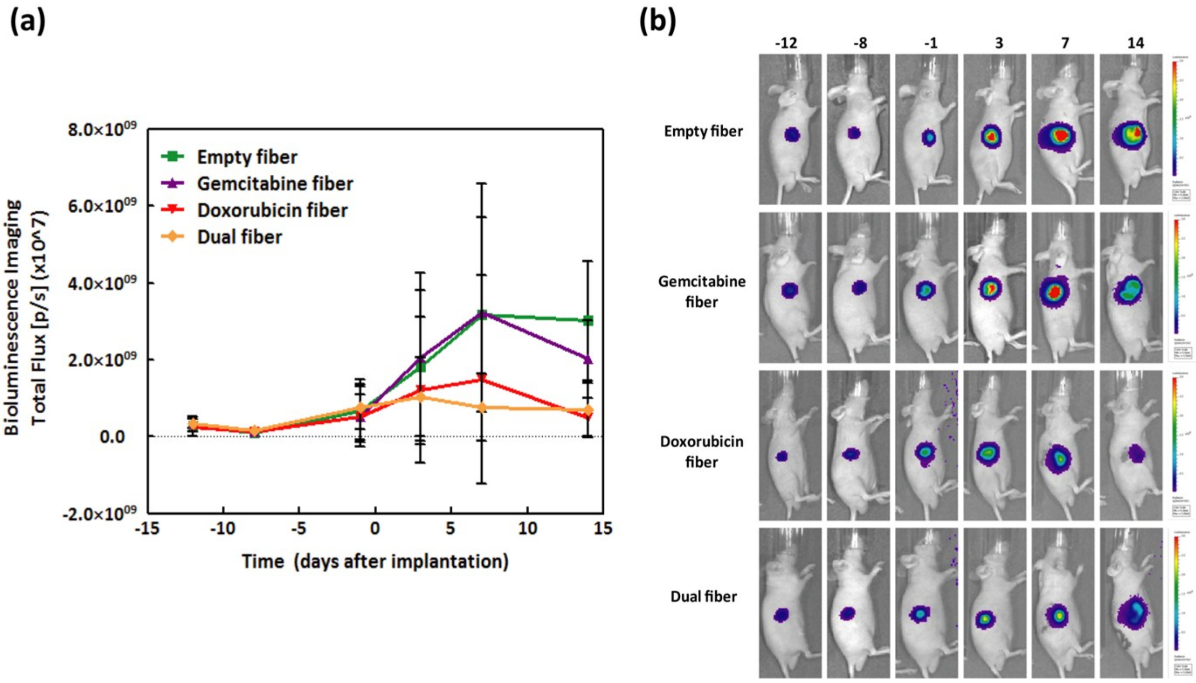

Figure S8. Therapeutic effect of drug loaded CS fibers in subcutaneous BxPC3-Luc tumor model. **(a)** Quantitative imaging data of BxCP3-Luc tumor growth presented as mean ± SD. **(b)** In vivo luciferase images of growing subcutaneous pancreatic tumors (IVIS Spectrum).

Table S1. Hydrodynamic dimeter, poly-dispersity index (PDI), and zeta potential of various formulations (n = 5, mean ± SD).

Formulation	Hydrodynamic diameter (nm)	PDI	Zeta potential (mV)
Alginate	110.9 ± 0.24	0.235 ± 0.007	-28.8 ± 0.36
Alginate+DOX	140.1 ± 0.49	0.196 ± 0.003	-30.4 ± 0.94
Alginate+GEM	126.2 ± 1.53	0.185 ± 0.015	-30.5 ± 0.30
Alginate-methacrylate	205.7 ± 0.40	0.348 ± 0.017	-29.9 ± 0.78
Alginate-methacrylate+DOX	239.0 ± 0.73	0.440 ± 0.024	-30.9 ± 0.67
Alginate-methacrylate+GEM	220.2 ±0.55	0.389 ±0.014	-30.4 ± 0.68
Alginate-dopamine	192.8 ± 1.83	0.352 ± 0.006	-33.2 ± 0.86
Alginate-dopamine+DOX	422.0 ± 0.24	0.383 ± 0.036	-37.2 ± 0.69
Alginate-dopamine+GEM	388.0 ± 0.35	0.465 ± 0.006	-34.0 ± 0.69

Table S2. Hematologic parameters from MIA PaCa-2 tumor bearing mice in various treatment groups. Data are presented as average ± SD (n = 5). WBC: white blood cell, RBC: red blood cell, HGB: hemoglobin, HCT: hematocrit, PLT: platelet, Neut: neutrophils, Lymp: lymphocytes, Mono: monocytes, Luc: large unstained cells.

Hematology	Unit	No treatment	Doxorubicin bolus		Gemcitabine bolus		Dual bolus		Empty fiber		Doxorubicin fiber		Gemcitabine fiber		Dual fiber	
			Day 3	Day14	Day 3	Day14	Day 3	Day14	Day 3	Day14	Day 3	Day14	Day 3	Day14	Day 3	Day14
WBC	10e3/uL	3.97±0.53	5.87±0.86	6.85±0.46	3.20±0.37	5.84±0.73	3.06±0.77	6.98±1.52	3.75±0.91	4.52±0.65	4.57±1.11	5.24±1.27	3.41±1.29	5.02±0.50	4.79±1.17	4.02±0.51
RBC	10e6/uL	10.08±0.07	9.93±0.23	9.81±0.26	9.98±0.27	9.99±0.35	10.20±0.32	10.40±0.29	10.07±0.21	10.20±0.26	10.46±0.33	5.42±0.75	9.88±0.32	9.29±1.27	9.66±0.34	10.07±0.24
HGB	g/dL	15.00±0.43	14.95±0.10	15.20±0.33	14.86±0.34	15.26±0.27	15.16±0.27	15.64±0.26	14.88±0.56	15.10±0.52	15.43±0.50	13.8±1.16	15.23±0.23	14.05±1.84	14.80±0.27	14.80±0.44
HCT	%	50.13±0.70	49.78±1.36	49.38±1.46	48.26±1.40	50.48±1.30	48.18±1.20	51.94±0.78	48.20±1.76	51.33±1.44	50.00±1.75	47.2±3.89	49±0.72	50.00±1.55	47.38±1.23	50.53±1.96
PLT	10e3/uL	996.75± 73.51	692.25± 212.99	961.80± 258.09	705.00± 73.71	1100.40± 195.05	704.20± 225.01	1215.60± 185.03	1252.5± 217.40	1037.67± 216.16	1417.00± 211.50	1266.25± 189.59	900.33± 102.96	1032.00± 159.61	911.25± 52.78	1239.33± 68.50
Neut	10e3/uL	1.46±0.12	2.41±0.29	2.39±0.53	0.79±0.26	2.32±0.30	0.59±0.16	2.98±0.48	1.20±0.41	2.34±0.66	3.89±1.76	3.45±0.93	1.29±0.91	2.41±7.95	2.67±0.82	2.54±0.44
Lymph	10e3/uL	2.30±0.47	2.85±0.91	3.30±1.02	2.04±0.48	2.90±0.88	2.17±0.80	3.36±1.30	2.26±0.55	1.94±0.07	1.85±0.51	1.50±0.49	1.88±0.27	1.85±0.29	1.90±0.51	1.21±0.11
Mono	10e3/uL	0.07±0.02	0.22±0.06	0.25±0.04	0.08±0.02	0.32±0.09	0.06±0.01	0.40±0.07	0.09±0.03	0.08±0.04	0.03±0	0.12±0.02	0.07±0.02	4.07±7.95	0.03±0.01	0.08±0.01
Luc	10e3/uL	0.04±0.01	0.03±0.01	0.01±0.01	0.02±0.01	0.02±0.01	0.05±0.02	0.02±0.01	0.13±0.01	0.06±0.01	0.04±0.02	0.06±0.02	0.12±0.08	0.04±0.02	0.14±0.04	0.05±0.01

Video S1. Video showing the fabrication process of drug loaded coaxial hydrogel fibers through wet-spinning process.

Video S2. Movie showing the swelling of drug loaded coaxial hydrogel fibers in SBF

References

[1] C. Lee, J. Shin, J.S. Lee, E. Byun, J.H. Ryu, S.H. Um, D.-I. Kim, H. Lee, S.-W. Cho, Bioinspired, calcium-free alginate hydrogels with tunable physical and mechanical properties and improved biocompatibility, Biomacromolecules 14(6) (2013) 2004-2013.