Electronic Supplementary Information Nanoparticle-Infused-Biodegradable-Microneedles as Drug-Delivery Systems

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Table S1 – Characterisation of Plain Silica Nanoparticles by TEM and DLS

	Size by TEM (nm)	Size by DLS (nm)	Zeta-Potential (mV)	PdI
NP1	70.56	105.7	-33.83	0.0583
NP2	61.94	111.3	-32.60	0.0613
NP3	87.11	111.3	-24.10	0.0643

Table S2 – Characterisation of FITC-doped Silica Nanoparticles by TEM and DLS

	Size by TEM (nm)	Size by DLS (nm)	Zeta-Potential (mV)	PdI
NP1	90	91.28	-42.40	0.0683
NP2	80	91.28	-32.33	0.0490
NP3	80	105.7	-37.37	0.0647

Figure S1 – Degradation of FITC-doped silica nanoparticles in PBS at 37°C

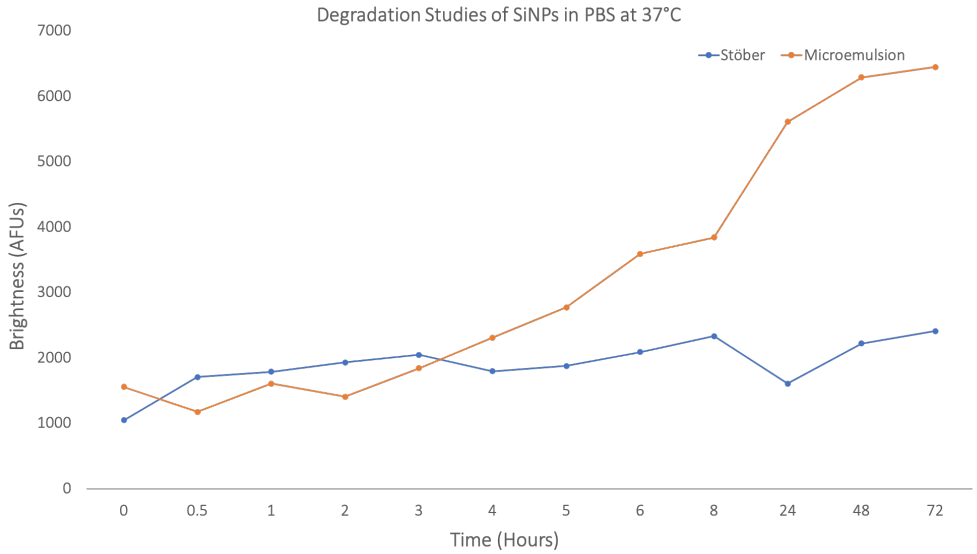


Figure S2 – Degradation of FITC-doped silica nanoparticles in BSA at 37°C

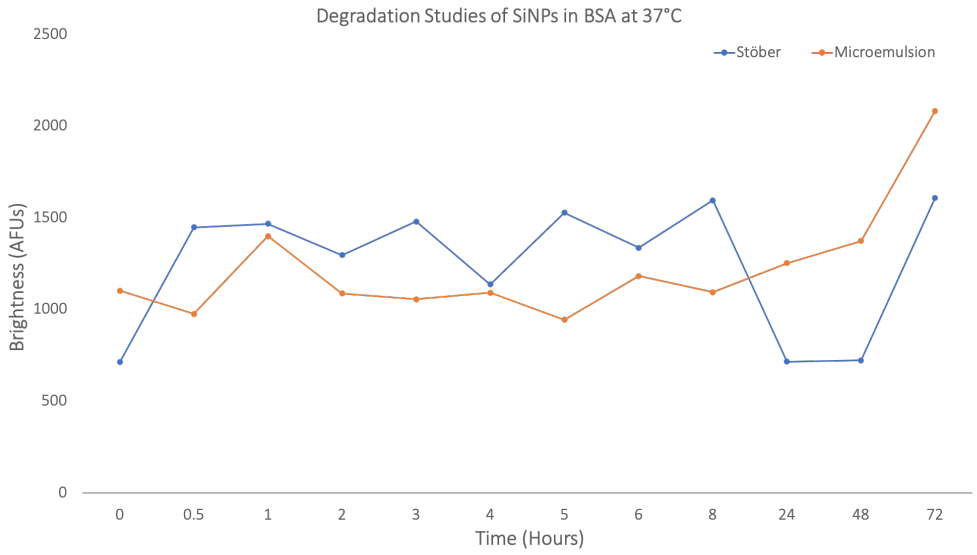


Table S3 – Initial Masses of Different w/w% of Anti-Cancer Drugs for Nanoparticle Synthesis

w/w%	DOX (mg)	TMZ (mg)	5-FU (mg)	PAC (mg)
1	1.25	0.42	0.28	1.83
2	2.49	0.83	0.56	3.65
3	3.73	1.25	0.84	5.48
4	4.97	1.66	1.11	7.31
5	6.22	2.08	1.39	9.14

Table S4 – Characterisation of Doxorubicin-doped Silica Nanoparticles by DLS

w/w%	Size by DLS (nm)	Zeta-Potential (mV)	PdI	Loading Efficiency (%)	Encapsulation Efficiency (%)
1	190.1	-26.70	0.4413	0.04	0.07
2	234.2	-41.05	0.2627	0.24	0.25
3	222.6	-28.30	0.5512	0.03	0.02
4	157.3	-37.83	0.5493	2.18	0.58
5	117.7	-40.67	0.1715	0.68	0.28

Table S5 – Characterisation of Temozolomide-doped Silica Nanoparticles by DLS

w/w%	Size by DLS (nm)	Zeta-Potential (mV)	PdI	Loading Efficiency (%)	Encapsulation Efficiency (%)
1	134.9	-28.70	0.2603	1.37	3.27
2	137.7	-32.45	0.1573	2.45	2.73
3	195.8	-34.08	0.0988	1.99	1.41
4	200.8	-31.15	0.1367	3.70	1.56
5	141.1	-34.03	0.1475	2.14	0.92

Table S6 – Characterisation of 5-Fluorouracil-doped Silica Nanoparticles by DLS

w/w%	Size by DLS (nm)	Zeta-Potential (mV)	PdI	Loading Efficiency (%)	Encapsulation Efficiency (%)
1	174.5	-26.03	0.1688	2.13	3.94
2	162.1	-46.70	0.1540	4.03	4.38
3	190.8	-25.17	0.1118	8.58	4.54
4	195.8	-27.28	0.0837	7.05	2.85
5	109.7	-34.57	0.1685	5.15	2.23

Table S7 – Characterisation of Paclitaxel-doped Silica Nanoparticles by DLS

w/w%	Size by DLS (nm)	Zeta-Potential (mV)	PdI	Loading Efficiency (%)	Encapsulation Efficiency (%)
1	116.8	-34.37	0.8393	3.85	1.15
2	207.9	-35.28	0.4278	1.35	0.83
3	163.1	-35.95	0.1093	0.23	0.13
4	180.2	-25.72	0.1363	0.70	0.25
5	142.8	-21.68	0.1310	0.15	0.06

Table S8 – Characterisation of Anti-cancer Drug-doped Silica Nanoparticles by TEM

	DOX-NPs	TMZ-NPs	5-FU-NPs	PAC-NPs
Size (nm)	39.95	56.61	44.33	50.78

Figure S3 – Calibration curve of doxorubicin hydrochloride over concentration range 0.001-0.05 mg/mL

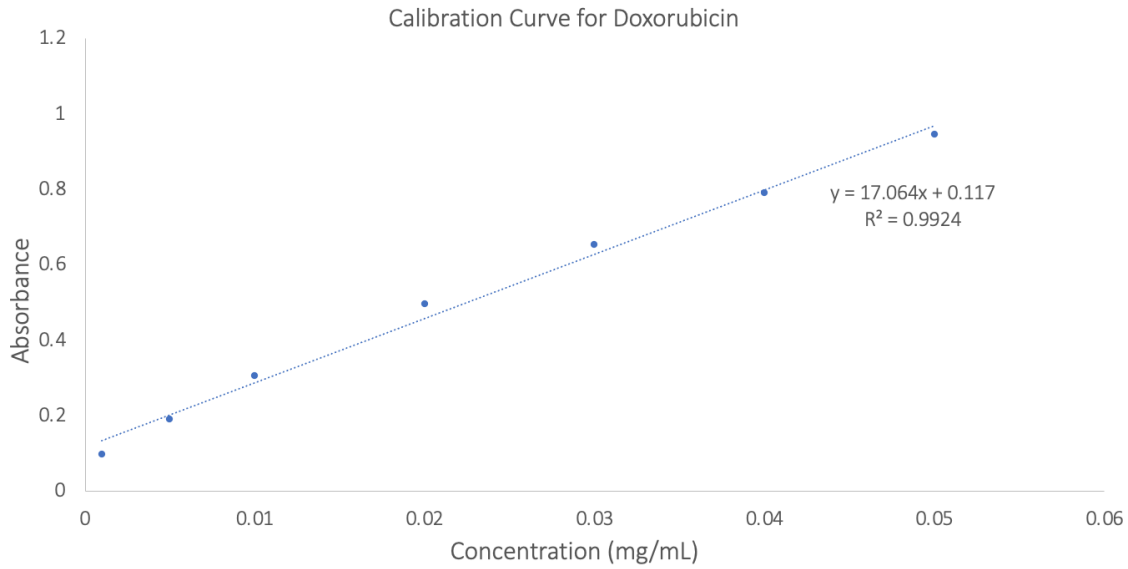


Figure S4 – Calibration curve of temozolomide over concentration range 0.01-0.04 mg/mL

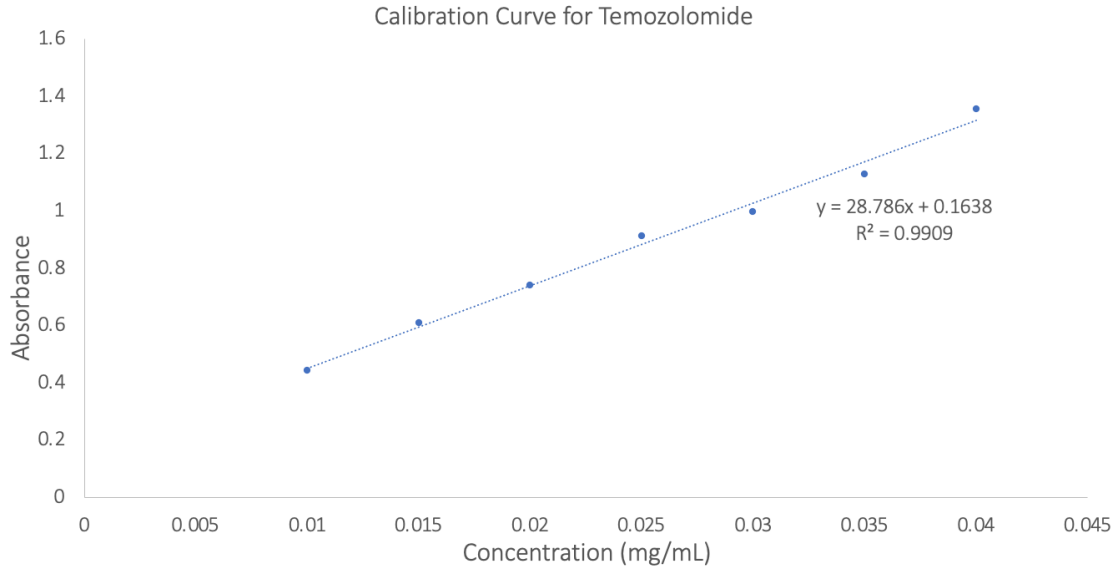


Figure S5 – Calibration curve for 5-fluorouracil over concentration range 0.005-0.1 mg/mL

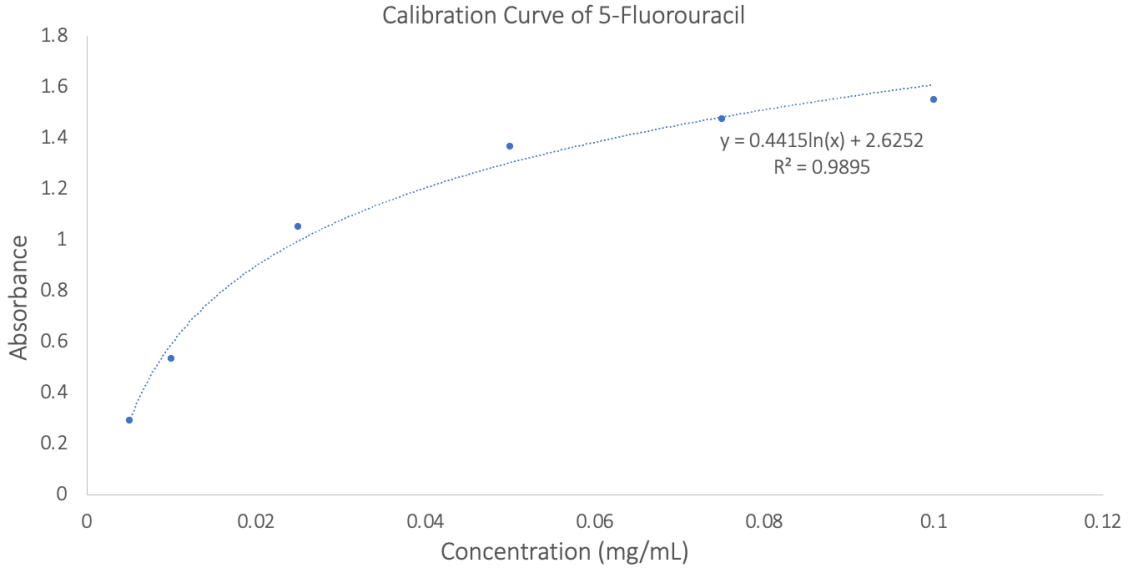


Figure S6 – Calibration curve for paclitaxel over concentration range 0.01-0.04 mg/mL

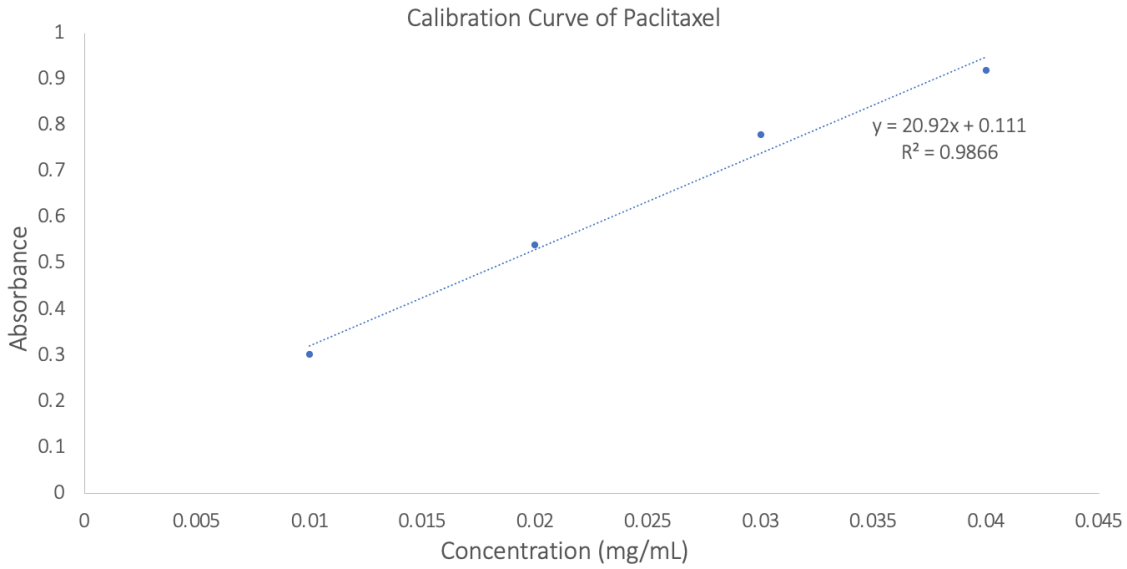


Table S9 – Characterisation of IgG Antibody-coated FITC-doped Silica Nanoparticles by DLS

	Size by DLS (nm)	Zeta-Potential (mV)	PdI
NP1	164.2	-13.30	0.3113
NP2	79.4	-16.03	0.8913
NP3	344.7	-10.27	0.1387

Table S10 – Characterisation of IgG Antibody-coated FITC-doped Silica Nanoparticles by TEM

	Core	Shell
Size (nm)	70.00	17.50

Figure S7 – Apparatus used for microneedle synthesis – a) microneedle mould; b) CMC-MAL gel solutions with FITC-doped silica nanoparticles of various concentrations incorporated into them

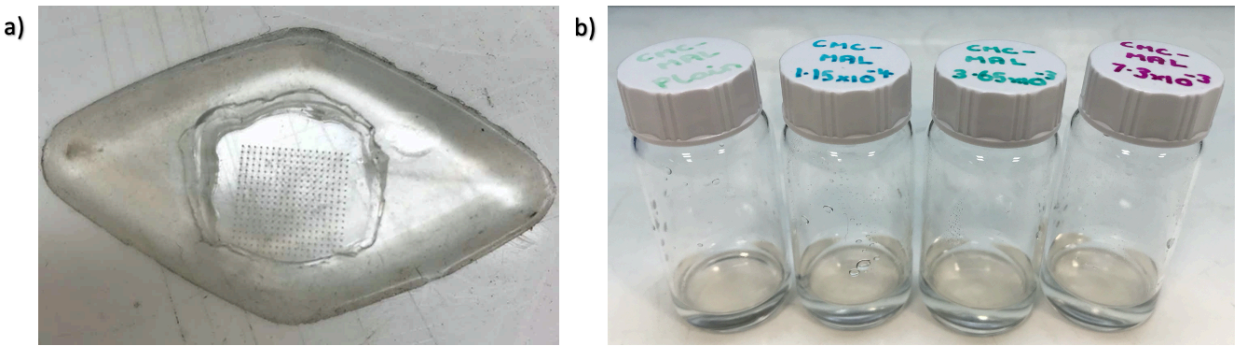


Figure S8 – Photos showing microneedle arrays after 6 months at room temperature

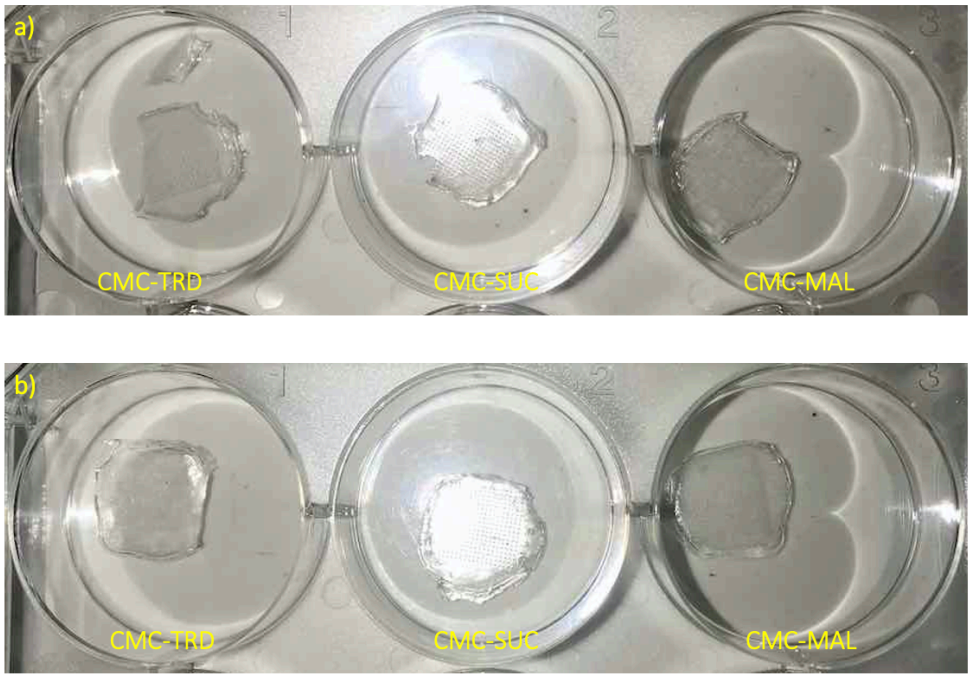


Figure S9 – Photos showing microneedle arrays after 6 months at 4°C

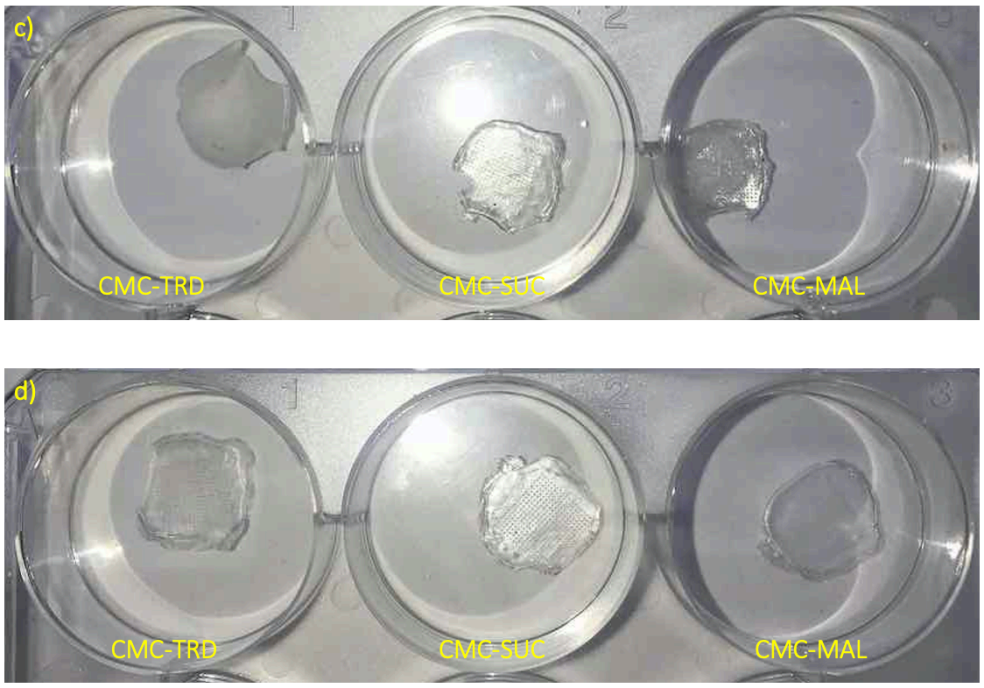


Figure S10 – Synthesis of microneedle arrays at various pressures – a) Gel solutions were inserted into moulds under vacuum and then sonicated before being placed into vacuum oven at various pressures to dry; b) Vacuum oven caused the gel solutions to bubble during drying leading to arrays like this one, where needles do not form at the bubbles as the gel isn't pulled down into the mould

Figure S11 – SEM images of gold nanoparticles in CMC-TRD arrays – a) Area of the array with multiple needles; b) Zoomed into needles to see gold nanoparticles in the tip of a needle

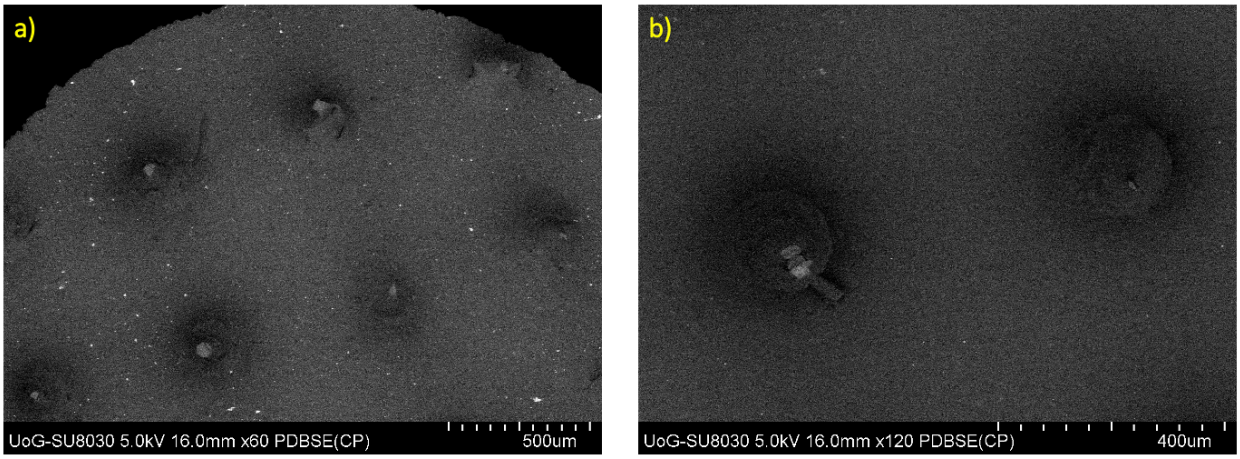


Figure S12 – SEM images of gold nanoparticles in CMC-SUC arrays – a) Area of the array with multiple needles; b) Zoomed into single needle to see a brighter tip where the gold nanoparticles are

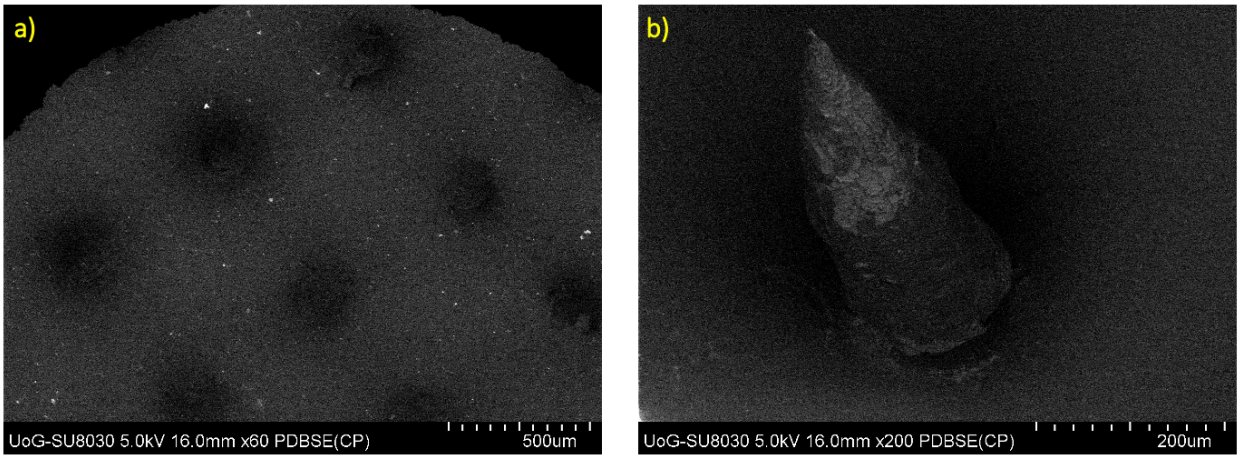


Figure S13 – SEM images of gold nanoparticles in CMC-MAL arrays – a) Area of the array with multiple needles; b) Zoomed into an area of single needles at the edge of the array with the backing plate

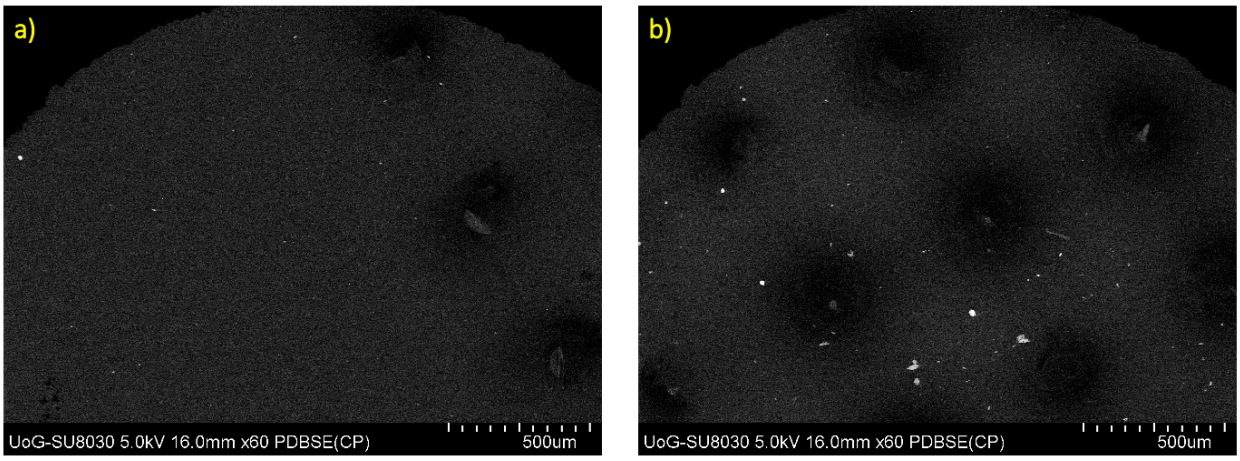


Figure S14 – FITC-SiNPs in Brine at **a)** 0 hours; **b)** 1 hour; **c)** 24 hours

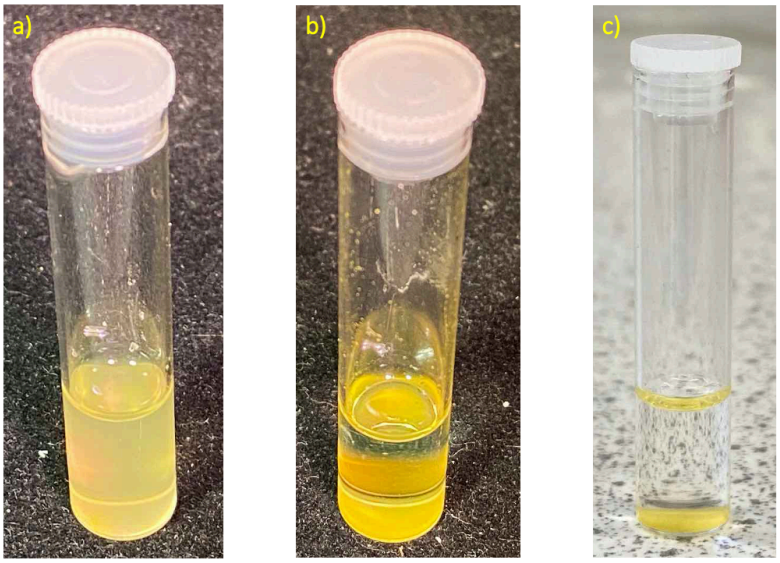


Figure S15 – Graph showing aggregation of FITC-SiNPs in Brine over 60 minutes

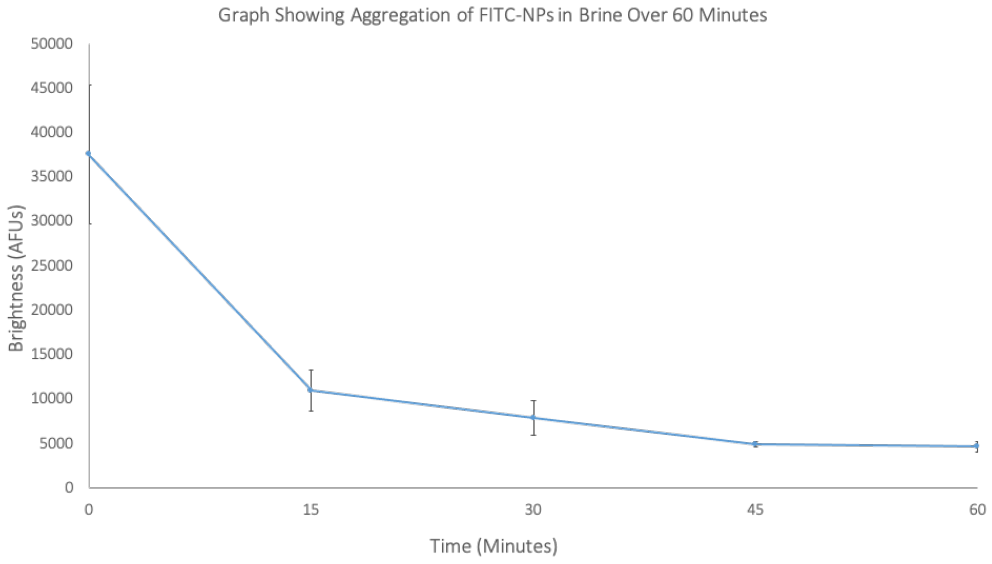


Figure S16 – FITC-SiNPs in CMC-TRD Gel with brine at **a)** 0 minutes; **b)** 60 minutes

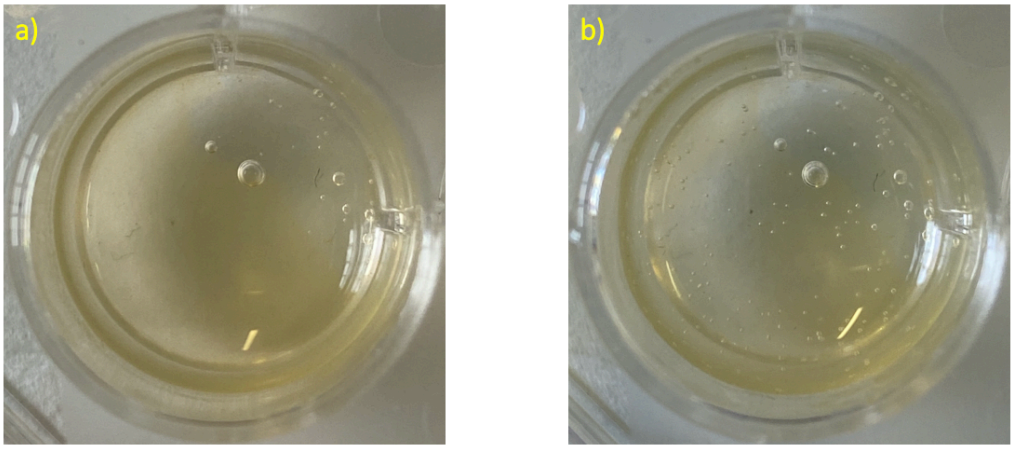


Figure S17 – Graph showing the stability of FITC-SiNPs in CMC-TRD gel with brine over 60 minutes

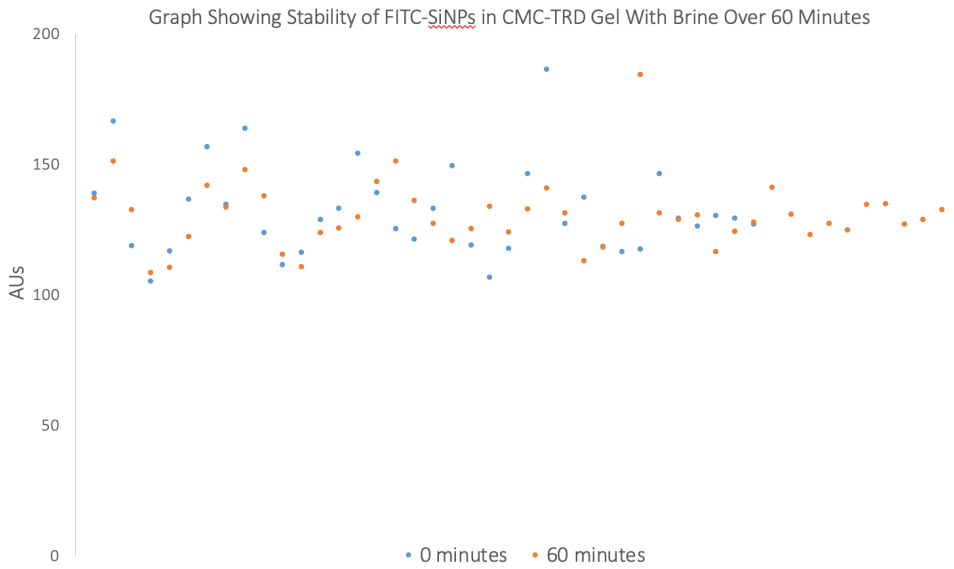


Figure S18 – Graph showing the stability of FITC-SiNPs in CMC-TRD gel over 4 hours

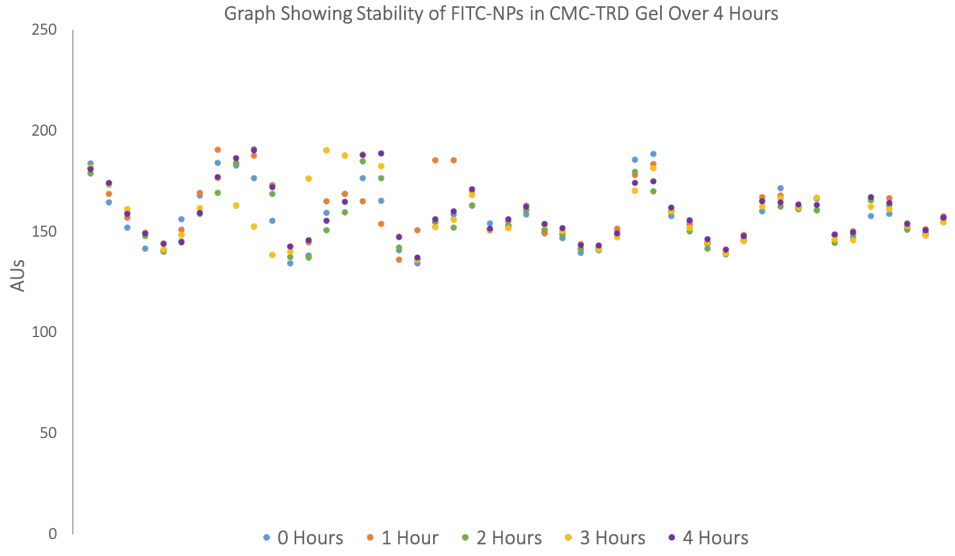


Figure S19 – FITC-SiNPs in CMC-TRD Gel with brine at **a)** 0 hour; **b)** 1 hour; **c)** 2 hours; **d)** 3 hours; **e)** 4 hours

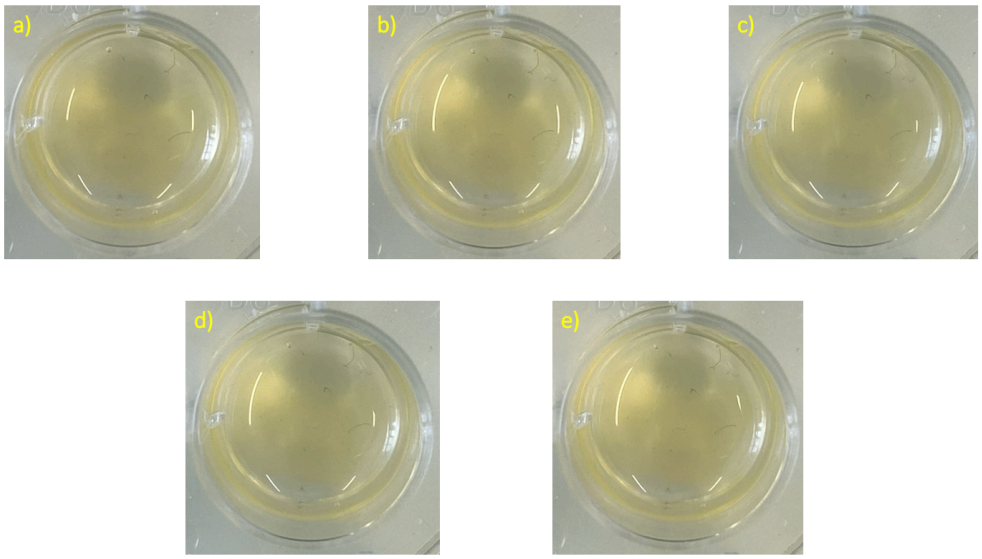


Figure S20 – Graph showing the degradation of microneedle arrays with FITC-SINPs encapsulated over 72 hours

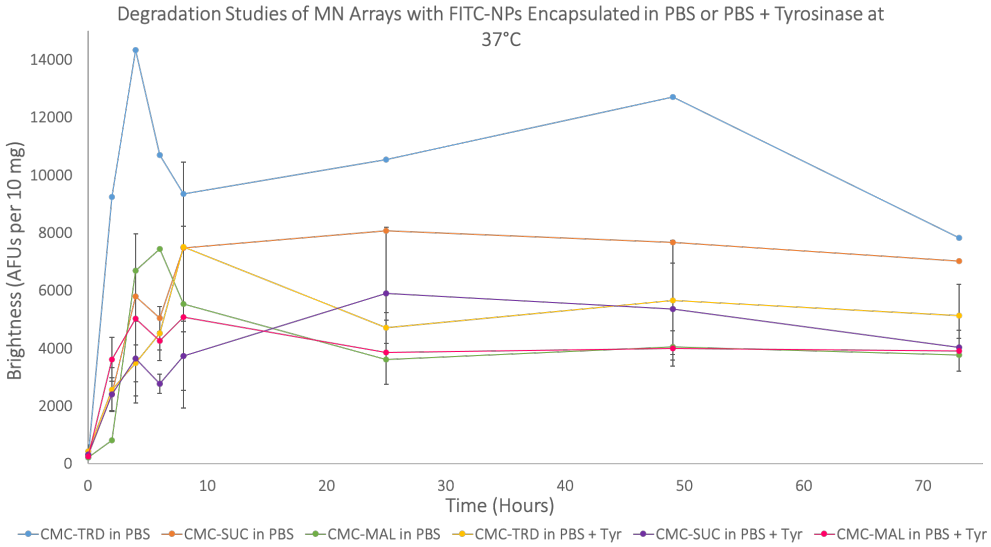


Figure S21 – Control experiments of degradation of FITC-SiNPs in PBS; FITC-SiNPs in PBS & tyrosinase; and tyrosinase in PBS

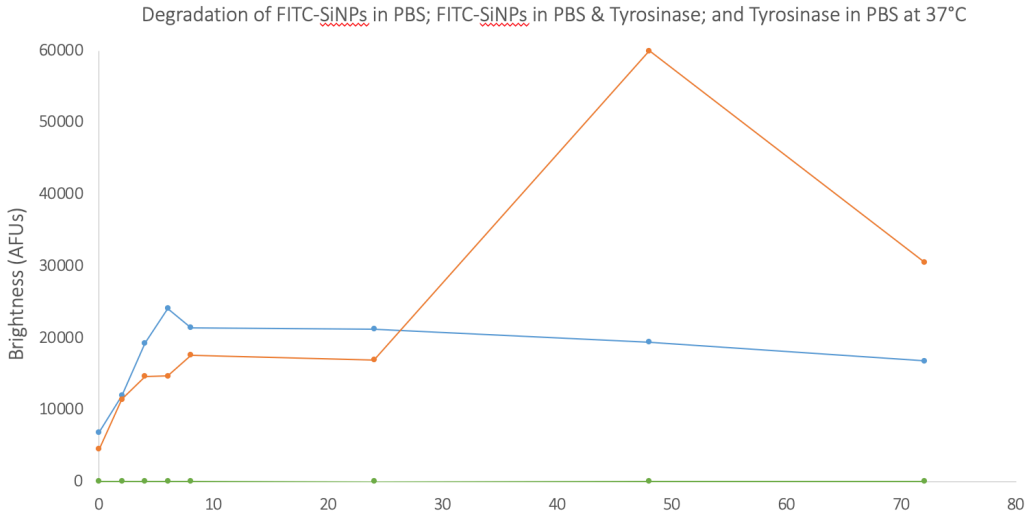


Figure S22 – Calibration curve of FITC in PBS and ethanol (90% v/v:10% v/v)

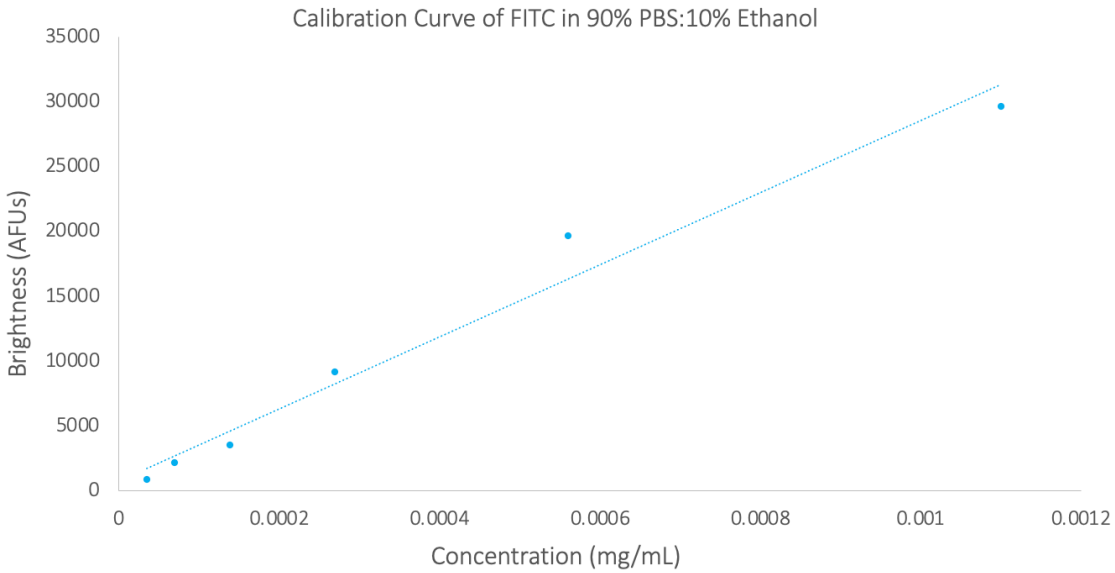


Figure S23 – Calibration curve of FITC-SiNPs in PBS

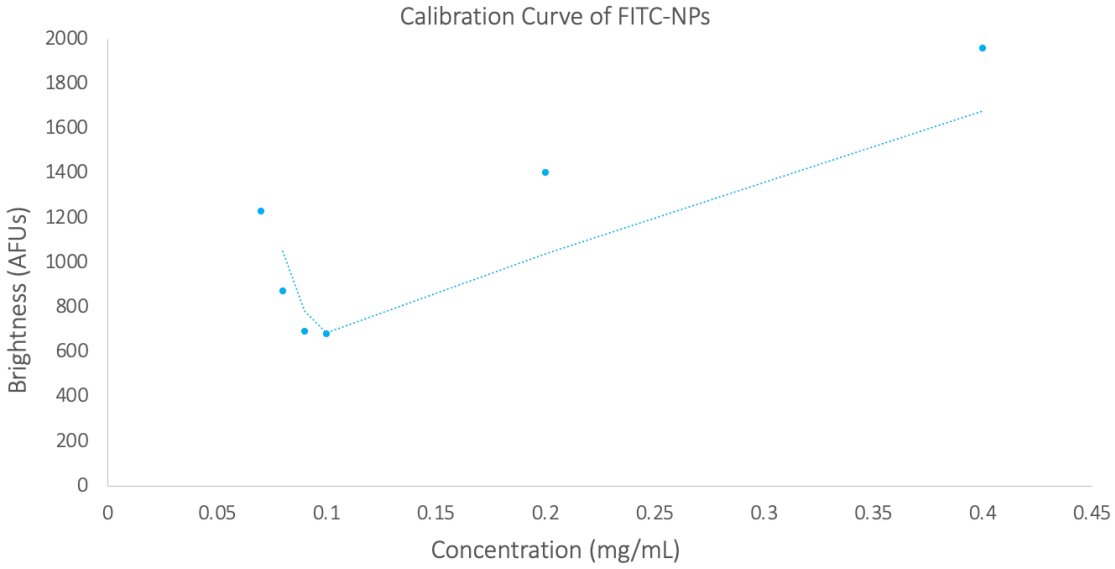


Figure S24 – Calibration curve of FITC-SiNPs in PBS repeated

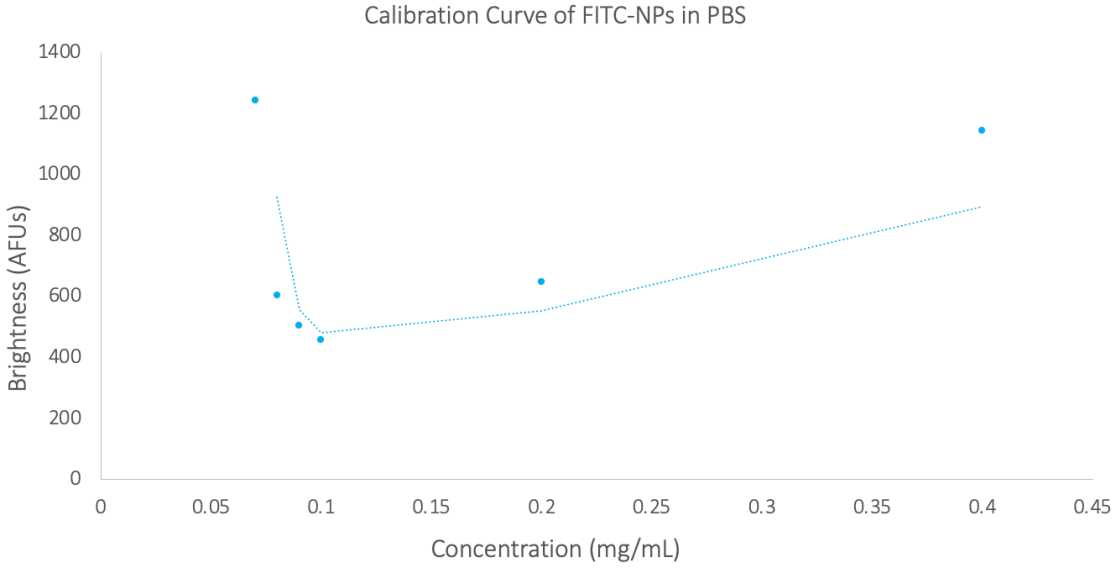
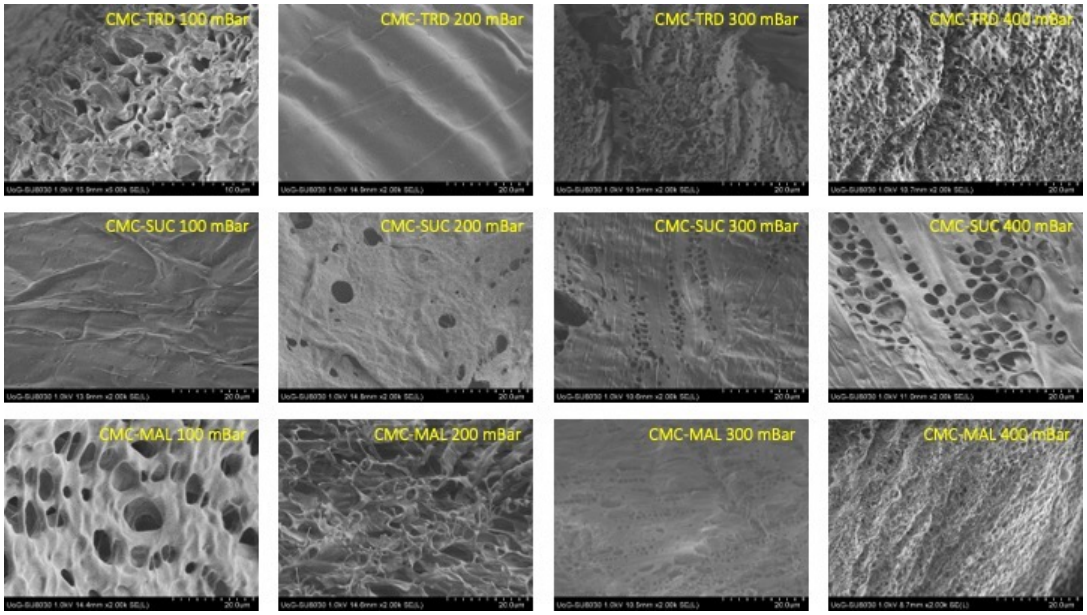


Figure S25 – SEM images of biodegradable microneedle gels formulated at various pressures – a) without silica nanoparticles; b) with silica nanoparticles

a)



b)

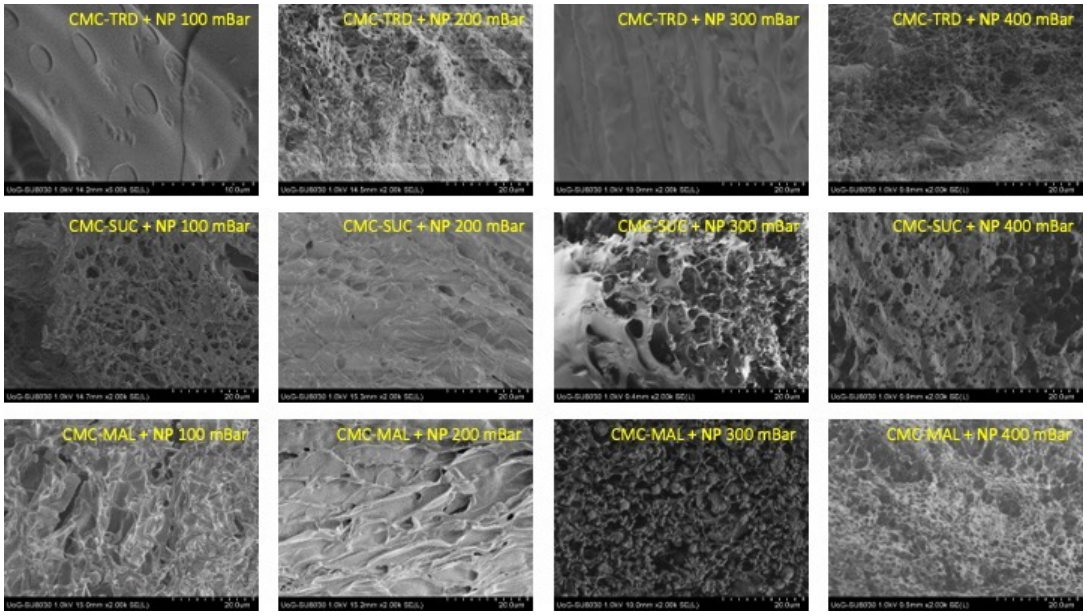


Table S11 – Gelation times of biodegradable microneedle gels formulated at various pressures with and without silica nanoparticles

Pressure (mBar)	CMC-TRD without NPs	CMC-TRD with NPs	CMC-SUC without NPs	CMC-SUC with NPs	CMC-MAL without NPs	CMC-MAL with NPs
100	3.5 hours	3 hours	3.5 hours	3 hours	3.5 hours	3 hours
200	7 hours	7 hours	5.5 hours	7 hours	7 hours	7 hours
300	8.5 hours	8.5 hours	8 hours	7.5 hours	8.5 hours	8.5 hours