Synthesis and Characterization of a Novel pH-Responsive Drug-Releasing Nanocomposite Hydrogel for Skin Cancer Therapy and Wound Healing

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Table S1. Dynamic light scattering analysis of PLGA-CMC NPs in terms of average diameter, surface charge and polydispersity index.

NP type	Size (nm)	Zeta-potential (mV)	Polydispersity index
PC-0.5	190 ± 8	-27.9 ± 0.3	0.05
PC-2.5	187 ± 13	-26.6 ± 0.4	0.17

Table S2. Low and high levels of formulation factors (PEGMC, PEGDA and TEMED) for the factorial design.

Factor	Units	Set values		Generated values			
		Low	High	Mean	Std. Dev.	Minimum	Maximum
PEGMC	mg/ml	100	200	150.00	42.39	65.91	234.09
PEGDA	mg/ml	50	100	75.00	21.20	32.96	117.04
TEMED	µL/ml	10	20	15.00	4.24	6.59	23.41
Note: APS was added at fixed ratios to TEMED: 8 mg per 10 µl TEMED.							

Table S3. Model selection with Design Expert software.

Study Type	Response Surface	**Subtype**	Randomized
Design Type	Central Composite	**Combination**	20
Design Model	Quadratic	**Blocks**	No Blocks

Table S4. A full-factorial design for the high and low values of the tested formulation factors. The half-factorial combination runs used in the experiments are highlighted in bold.

Combination	Factors

	PEGMC	PEGDA	TEMED
order	mg/ml	mg/ml	uL/mL
1	150	75	6.59
2	150	75	23.41
3	150	75	15
4	150	75	15
5	**200**	**100**	**10**
6	**200**	**50**	**20**
7	150	75	15
8	150	75	15
9	150	75	15
10	**200**	**50**	**10**
11	**100**	**100**	**10**
12	**200**	**100**	**20**
13	150	32.95	15
14	150	75	15
15	**100**	**100**	**20**
16	65.91	75	15
17	**100**	**50**	**20**
18	**100**	**50**	**10**
19	150	117.05	15

20	234.09	75	15

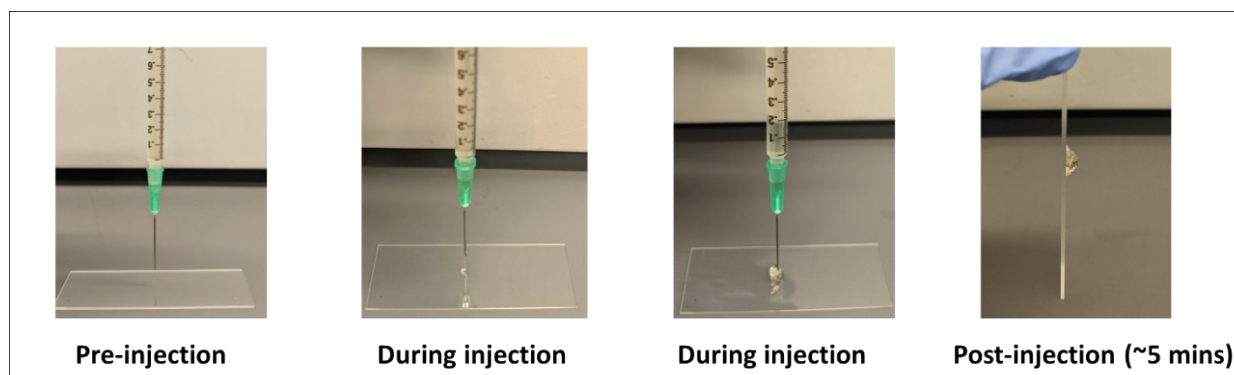Pre-injection | During injection | During injection | Post-injection (~5 mins)

Figure S1: Image of PEGMC hydrogel injection through a 21-G needle pre-, during and post injection, confirming injectability of the formulation. A clear hydrogel was formed, in comparison to NCH system, which was slightly cloudy due to the presence of the NPs.
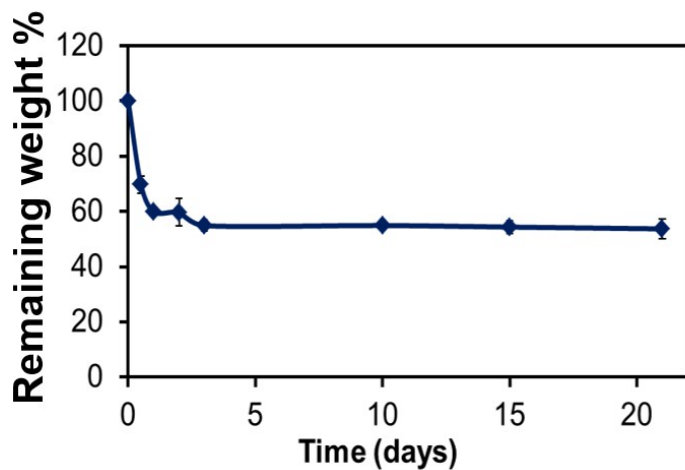

Figure S2: Degradation profile of NCH system studied over three weeks showing gradual degradation over time.