Electronic Supplementary Information (ESI)

An Injectable, Self-Healing, Polysaccharide-Based Antioxidative Hydrogel for Wound Healing

Melissa Johnson [a,b] Rijian Song,[a,b,c,d] Yinghao Li,[a] Cameron Milne,[a,b] Zishan Li,[a] Jing Lyu,[a] Sigen A,[a,b] and Wenxin Wang[a,c,d]*

[a] Charles Institute of Dermatology, School of Medicine, University College Dublin, D04 V1W8 Dublin, Ireland.

[b] Blafar Ltd, Pioneer Life Sciences Cherrywood, Cherrywood Business Park, Loughlinstown, D18 T3Y1 Dublin, Ireland.

[c] Joint Research Center for Occupational Medicine and Health of IHM, Anhui University of Science and Technology, Huainan, China.

[d] Institute of Precision Medicine (AUST-IPM), Anhui University of Science and Technology, Huainan, China

*Corresponding author:

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Supplementary Experimental Section

Synthesis of 3,3'-dithiobis(propanoic dihydrazide) (DTP)

DTP was synthesised according to a previously published protocol [1]. Briefly, 3,3'-Dithiodipropionic acid (20 g), absolute ethyl alcohol (200 mL), and two drops of sulfuric acid were added into a round bottom flask equipped with a condenser and the system was refluxed overnight until the raw material was fully consumed, monitored by Thin-layer chromatography (TLC) test. The ethyl alcohol was removed by rotary evaporator (rotavapor) and diethyl ether (300 mL) was added to dissolve the crude oil. The organic layer was washed by H_2O (3×200 mL) then the diethyl ether was removed by rotavapor to afford the crude diester (22.8 g) as colourless oil and the diester was used without further purification. Diester (20 g) and hydrazine hydrate (8 equiv.) were dissolved into ethyl alcohol (50 mL), respectively. The solution of diester was added into the solution of hydrazine hydrate dropwise under room temperature (RT). The reaction was heated to 50 °C and monitored by TLC until the reaction was completed, then the solution was cooled to RT. DTP was precipitated and filtered followed by washing with cold hexane to afford the white crystal. The final product was dried with vacuum oven for 2 days to fully remove the hydrazine hydrate (15.8 g, 88.1% yield). ^{1}H-NMR (400 MHz, DMSO-d6): δ=9.06 (s, 2H), δ=4.22 (s, 4H), δ=2.89 (t, 4H), δ=2.40 (t, 4H).

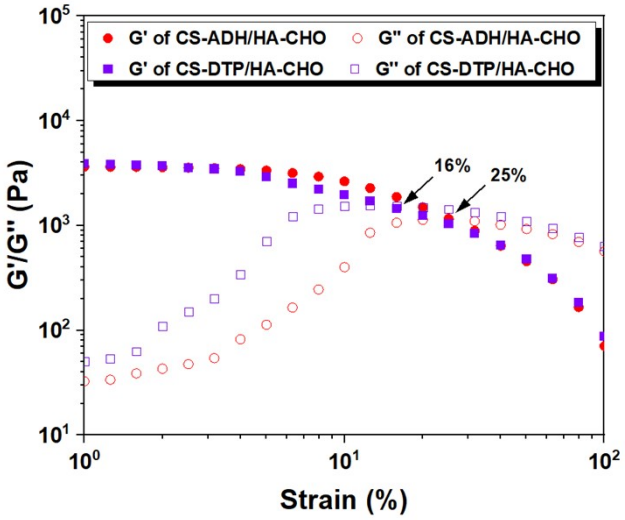

Figure S1: Strain-amplitude sweep test of CS-DTP/HA-CHO and CS-ADH/HA-CHO hydrogels at 2 hours (25 ˚C, and 1 Hz).

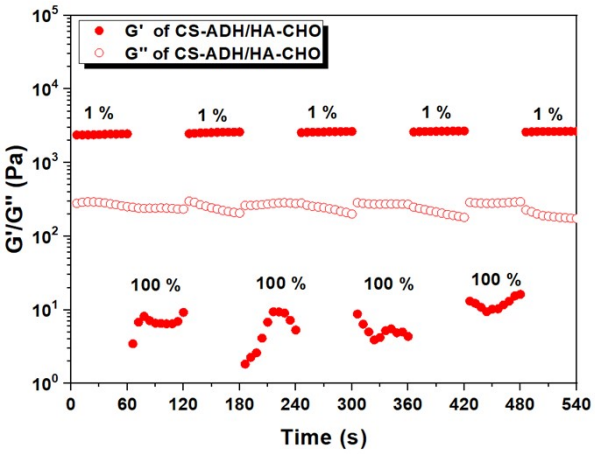

Figure S2: Oscillation step-strain test of applied strain from 1% to 100% for 540 seconds for CS-ADH/HA-CHO (25 ˚C, 1 Hz).

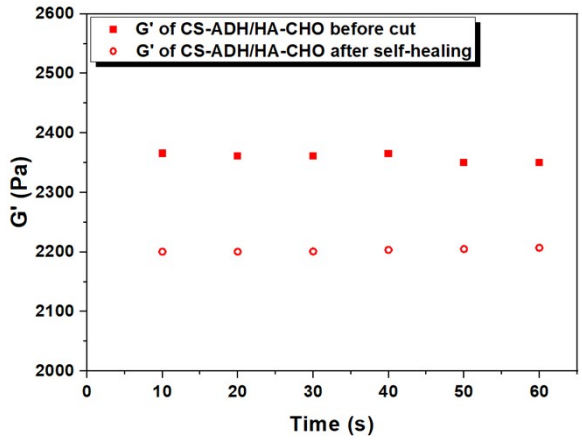

Figure S3: Mechanical property test, before cut and after self-healing of CS-ADH/HA-CHO.

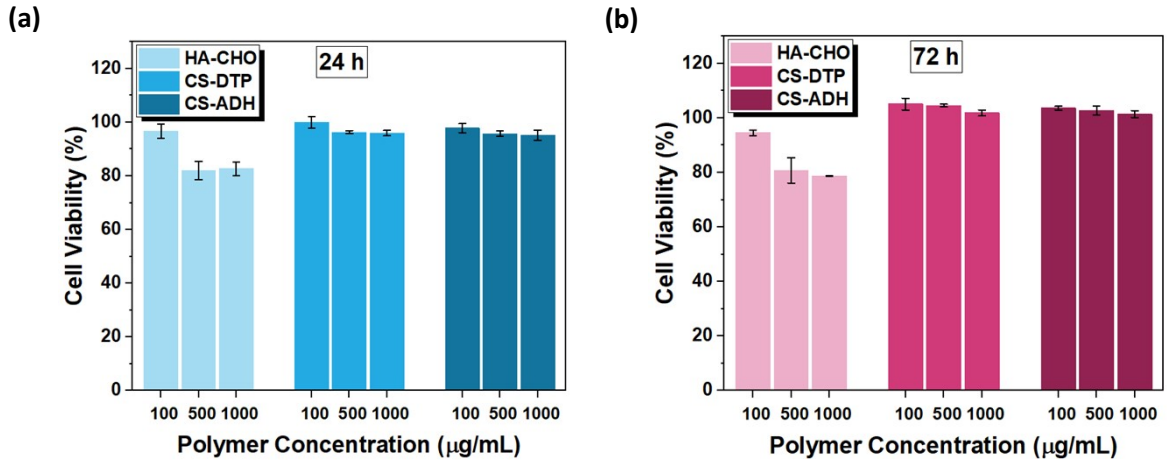

Figure S4: (a) Quantitative cell viability evaluation by alamarBlue assay of HA-CHO, CS-DTP and CS-ADH at different concentrations after 24 h co-culture with HaCaTs; (b) Quantitative cell viability evaluation by alamarBlue assay of HA-CHO, CS-DTP and CS-ADH at different concentrations after 72 h co-culture with HaCaTs.

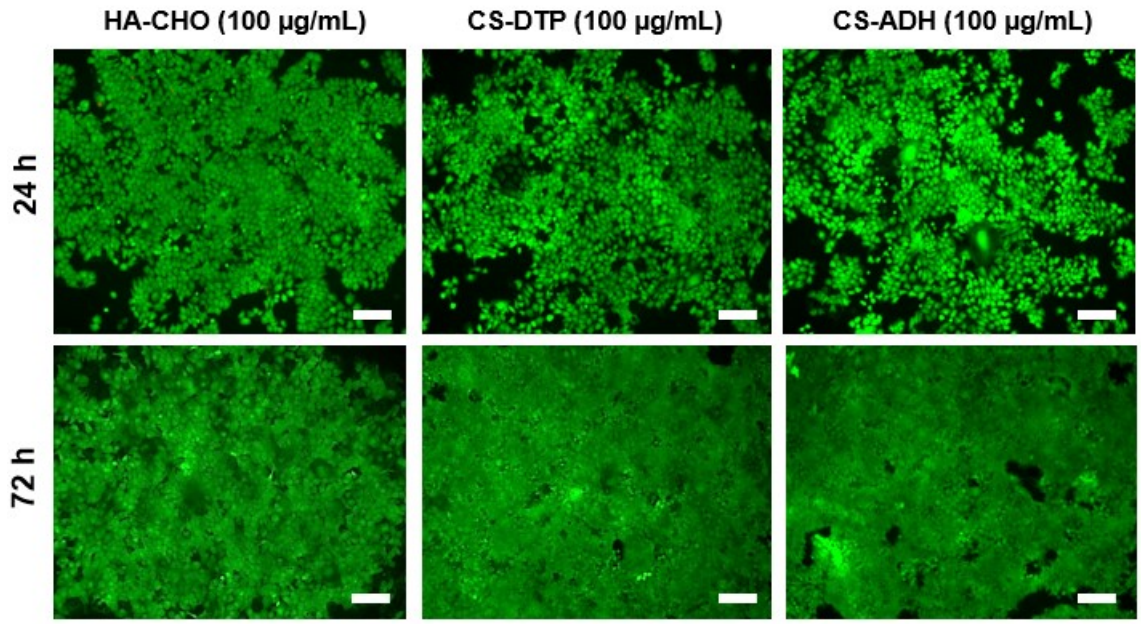

Figure S5: Representative LIVE/DEAD staining images of co-culture HaCaTs with HA-CHO, CS-DTP and CS-ADH (100 µg/mL) at 24 h and 72 h. Scale bar: 100 µm.

References

1 K. P. Vercruysse, D. M. Marecak, J. F. Marecek and G. D. Prestwich, Synthesis and in vitro degradation of new polyvalent hydrazide cross-linked hydrogels of hyaluronic acid, *Bioconjug. Chem.*, 1997, **8**, 686–694.