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A pH-responsive self-healing hydrogel based on multivalent coordination of Ni^{2+} with polyhistidine terminated PEG and IDA modified oligochitosan

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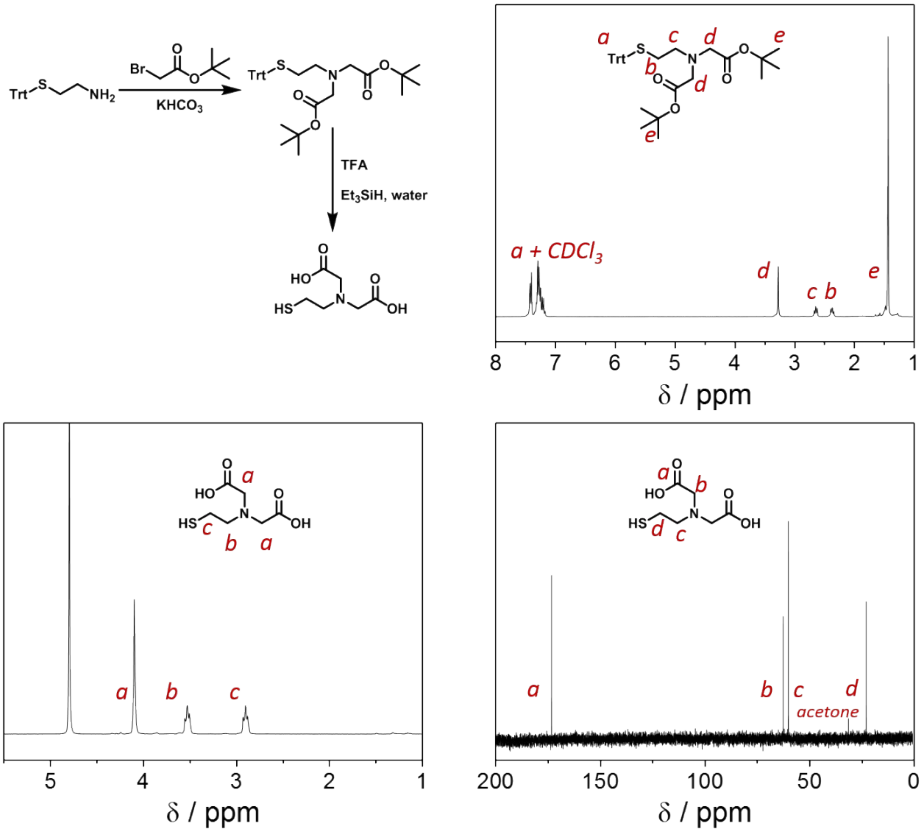

Fig. S1 Synthesis of the IDA-SH and related $^{1}H/^{13}C$ NMR characterization.

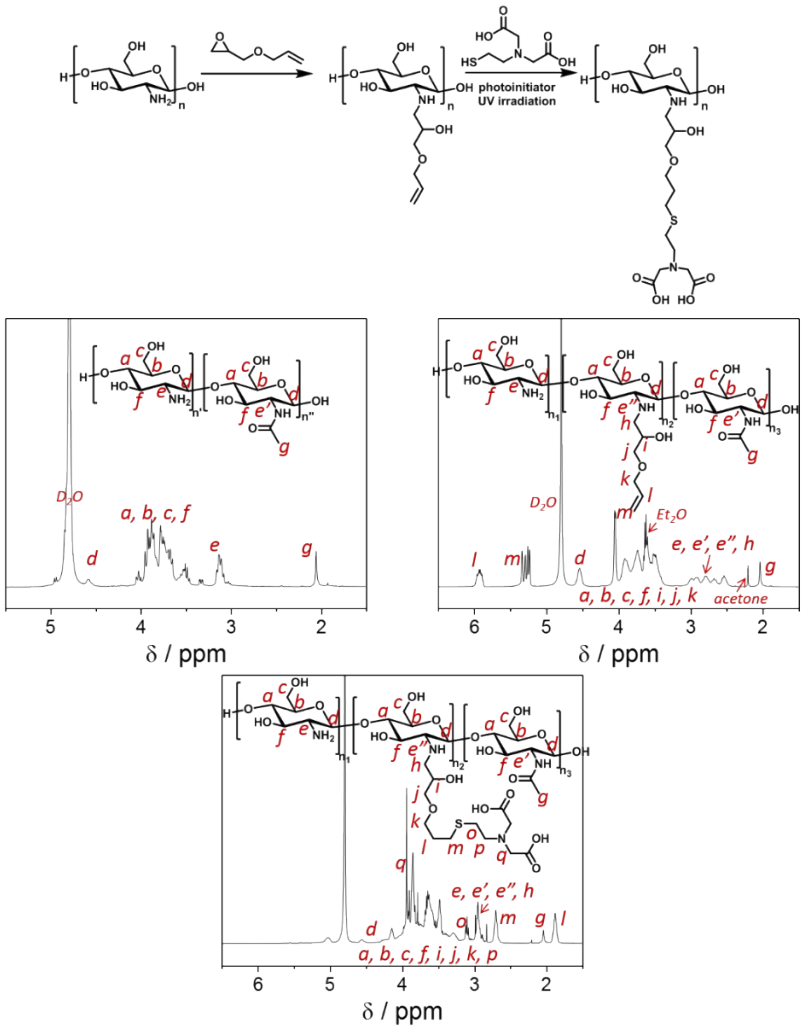

Fig. S2 Synthesis of the OChi-IDA and related ^{1}H NMR characterization.

From the ^{1}H NMR of oligochitosan, the deacetylation fraction was determined as 90.2%, which was calculated from the peak of the methyl moieties of acetamido groups (approx. 2.0 ppm, Peak *g*) and the multiplet peak of the hydrogens on the glycosidic ring (approx. 3.4-4.1 ppm, Peak *a*, *b*, *c*, *f*). Moreover, the modification efficiency of allyl modified oligochitosan was calculated form the peak of allyl group (approx. 5.3, 5.9 ppm, Peak *m*, *l*) and the peak of the methyl moieties of acetamido groups (approx. 2,0 ppm, Peak *g*), which was 79.2% without considering the acetylated glycosidic units. Finally, the efficiency of the thiol-ene reaction was determined by the disappearance of peaks attributed to the allyl groups, which indicated a full conversion for the thiol-ene click reaction.

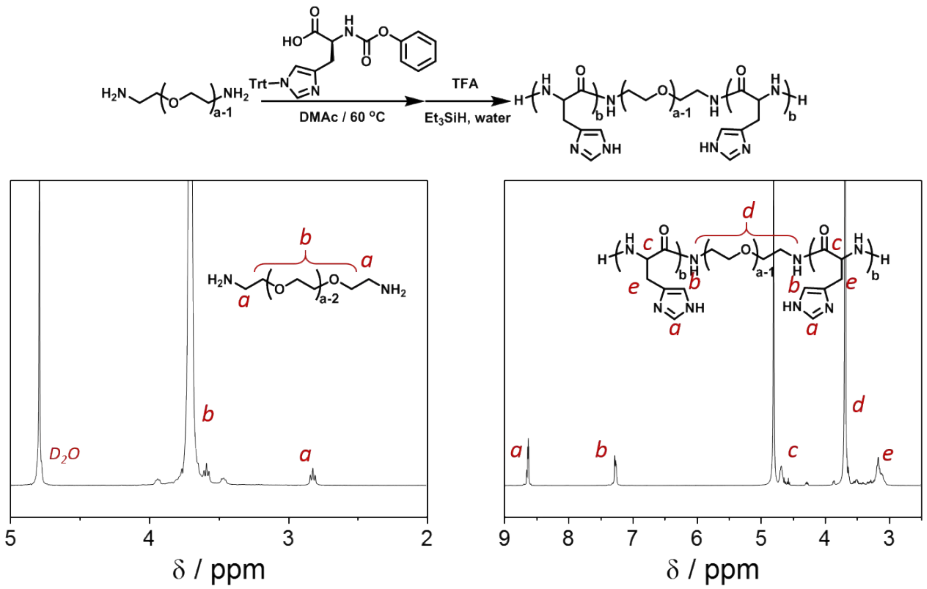

Fig. S3 Synthesis of the PEG-PHis$_{3,6,9}$ and related ^{1}H NMR characterization.

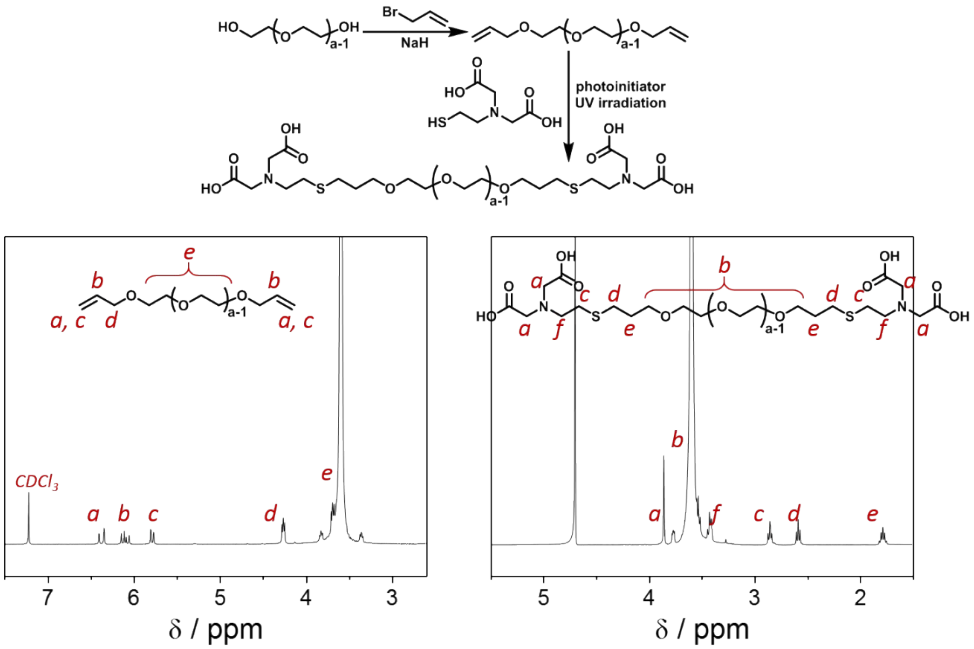

Fig. S4 Synthesis of the PEG-IDA and related ^{1}H NMR characterization.

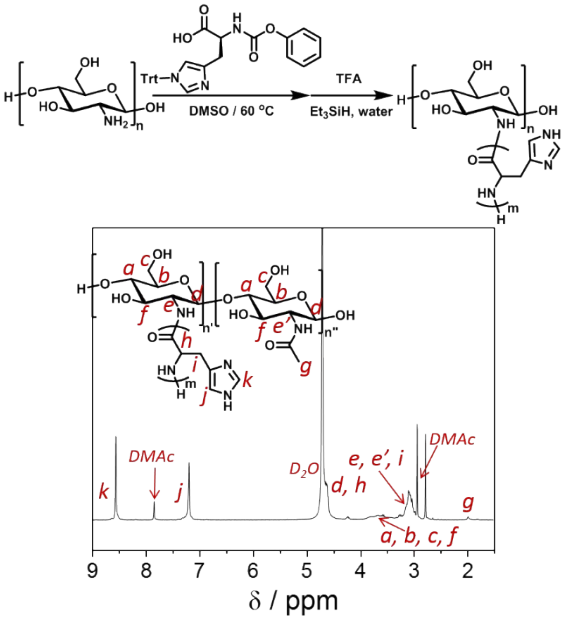

Fig. S5 Synthesis of the OChi-PHis$_6$ and related ^{1}H NMR characterization.

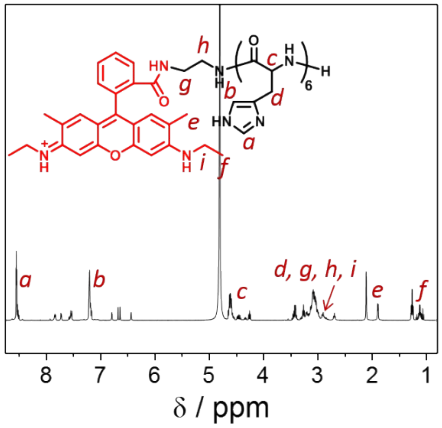

Fig. S6 ^{1}H NMR spectra for Rh6G-PHis$_{6}$.

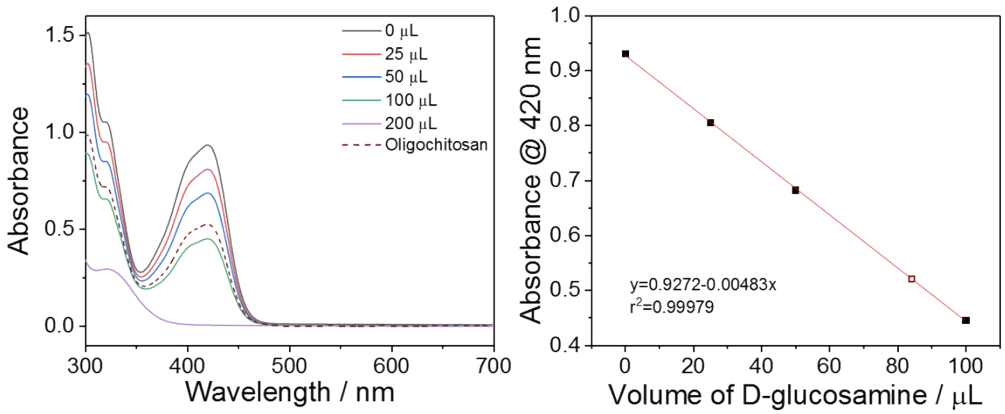

Fig. S7 Determination of molecular weight of the purchased oligochitosan (0.051 mg for the measurement) via end group analysis using UV-Vis spectrometer and its standard curve.

The core of the end group analysis is the determination of the molar concentration of the reductive end group in the precise amount of oligochitosan solution. By the above analysis, the end group concentration of the 0.051 mg oligochitosan is equal to 84 μL standard D-glucosamine solution. Thus, the molecular weight of the oligochitosan is 1307 g/mol, and the degree of polymerization is around 8.1. Due to the modification efficiency calculated above, the IDA groups per oligochitosan was approximately 5.8.

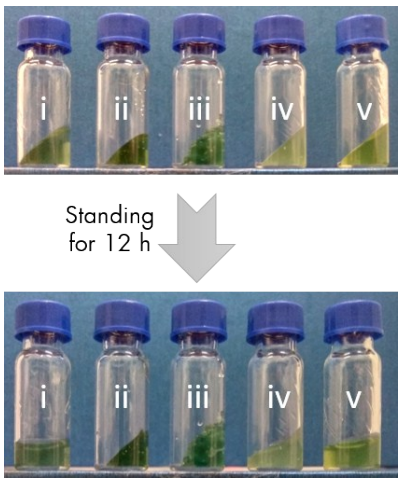

Fig. S8 Photos for the free-standing test for (i) OChi-IDA/PEG-PHis$_6$ (PHis:IDA = 1:1), (ii) OChi-IDA/PEG-PHis$_6$ (PHis:IDA = 1:2), (iii) OChi-IDA/PEG-PHis$_9$ (PHis:IDA = 1:3), (iv) OChi-*g*-PHis$_6$/PEG-IDA (PHis:IDA = 1:1) and (v) OChi-*g*-PHis$_6$/PEG-IDA (PHis:IDA = 1:2).

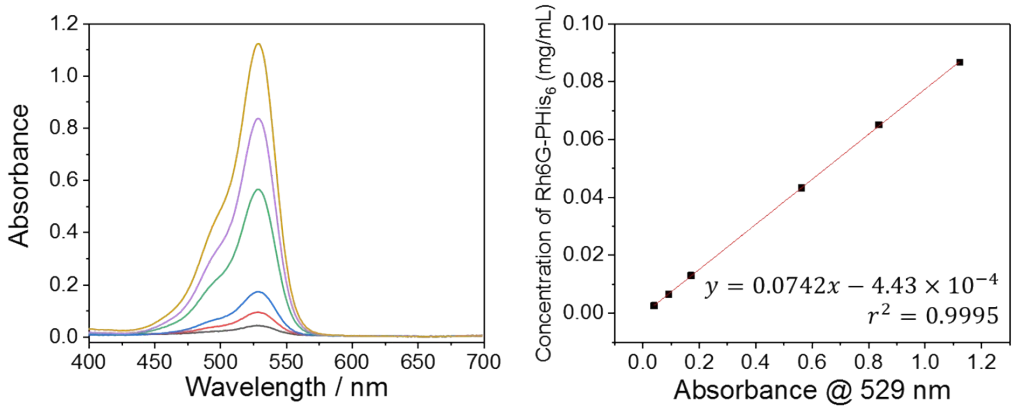

Fig. S9 Standard curve for the Rh6G-PHis$_6$ model molecule using the UV-Vis spectrometer.

Table S1 Exact dry weight of hydrogels in swelling tests.

Hydrogels	Buffers	Weight / mg		
OChi-*g*-PHis$_6$/PEG-IDA (PHis:IDA = 1:1)	pH 7.4	19.7	19.5	21.3
OChi-IDA/PEG-PHis$_6$ (PHis:IDA = 1:1)	pH 7.4	20.5	18.7	20.9
OChi-IDA/PEG-PHis$_6$ (PHis:IDA = 1:2)	pH 7.4	17.9	20.6	21.5
	pH 5.5	23.2	20.4	20.9
OChi-IDA/PEG-PHis$_9$ (PHis:IDA = 1:3)	pH 7.4	20.2	19.4	18.7
	pH 5.5	18.9	19.5	21.2
	pH 4.3	19.6	21.4	18.8

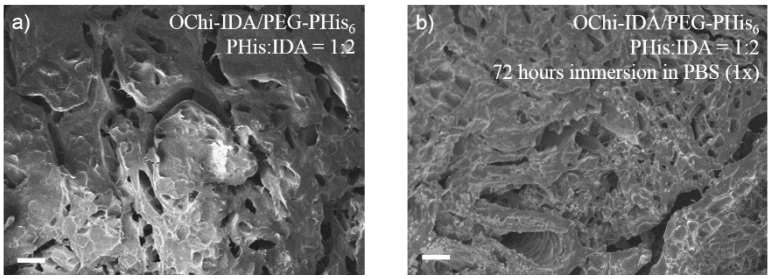

Fig. S10 SEM images of the OChi-IDA/PEG-PHis$_6$ (PHis:IDA = 1:2) hydrogel before and after 72 hours immersion in PBS (1x). Scale bars: 20 μm.

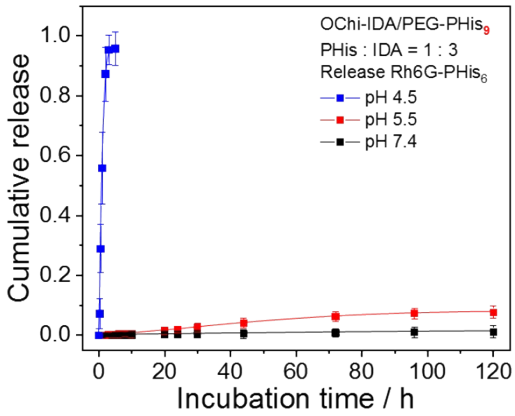

Fig. S11 The cumulative release of Rh6G-$PHis_6$ model molecule *versus* incubation time for the OChi-IDA/PEG-$PHis_9$ (PHis:IDA = 1:3) hydrogel in pH 7.4, 5.5 and 4.5 buffer. Each error bar presents mean ± SD, n = 3.

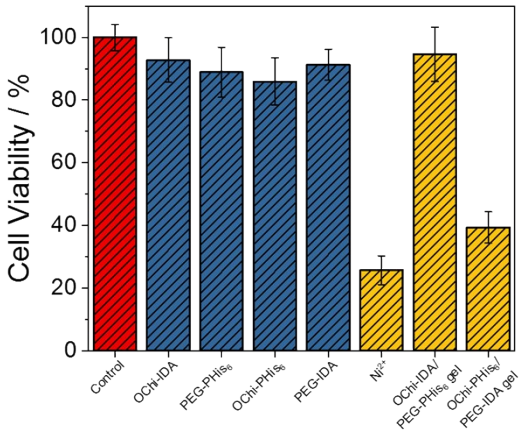

Fig. S12 In vitro cytotoxicity evaluation of OChi-IDA/PEG-$PHis_6$ (PHis:IDA = 1:2), OChi-$PHis_6$/PEG-IDA (PHis:IDA = 1:1) hydrogels and their components. Each bar presents mean ± SD, n = 5.