

# **Synthesis, Characterization and Stability of Crosslinked Chitosan-Maltodextrin pH-Sensitive Nanogels**

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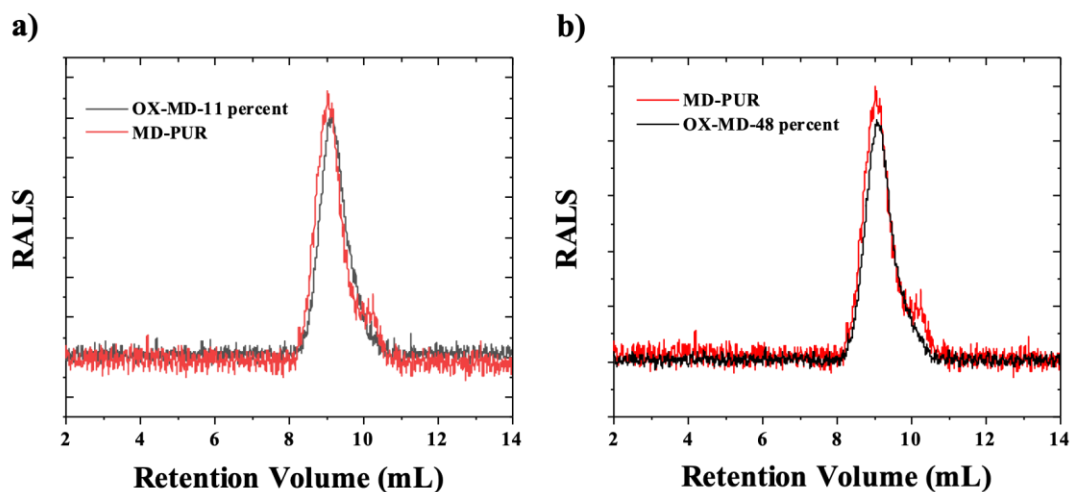
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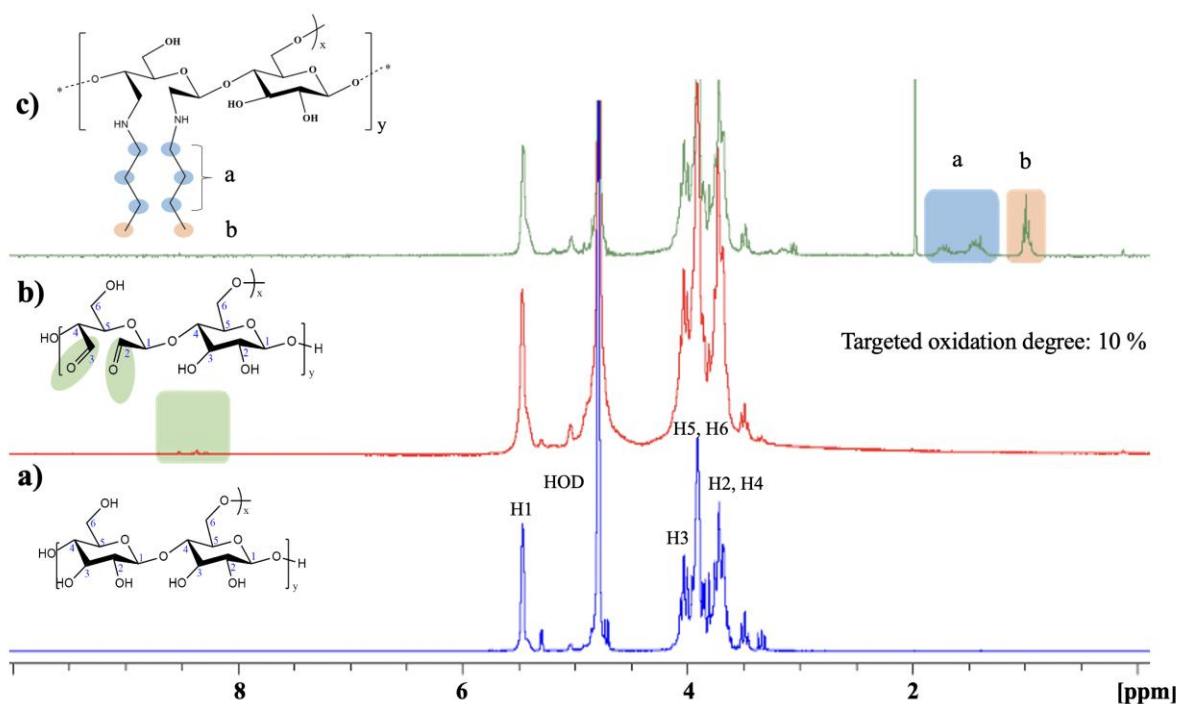
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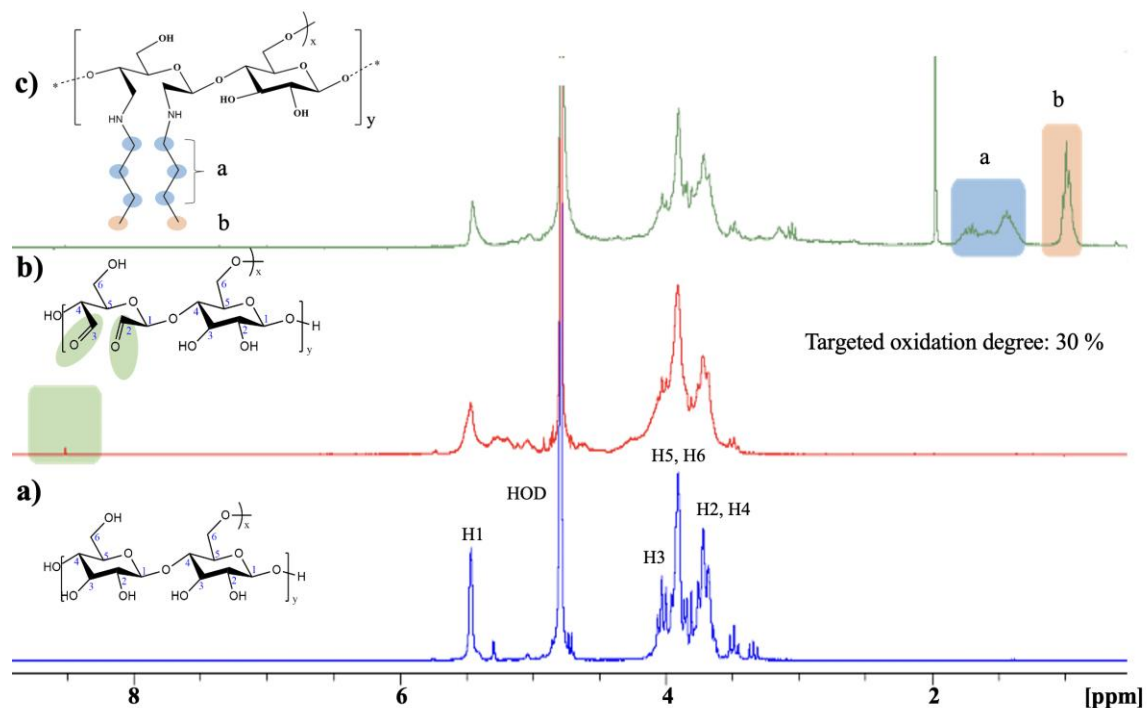
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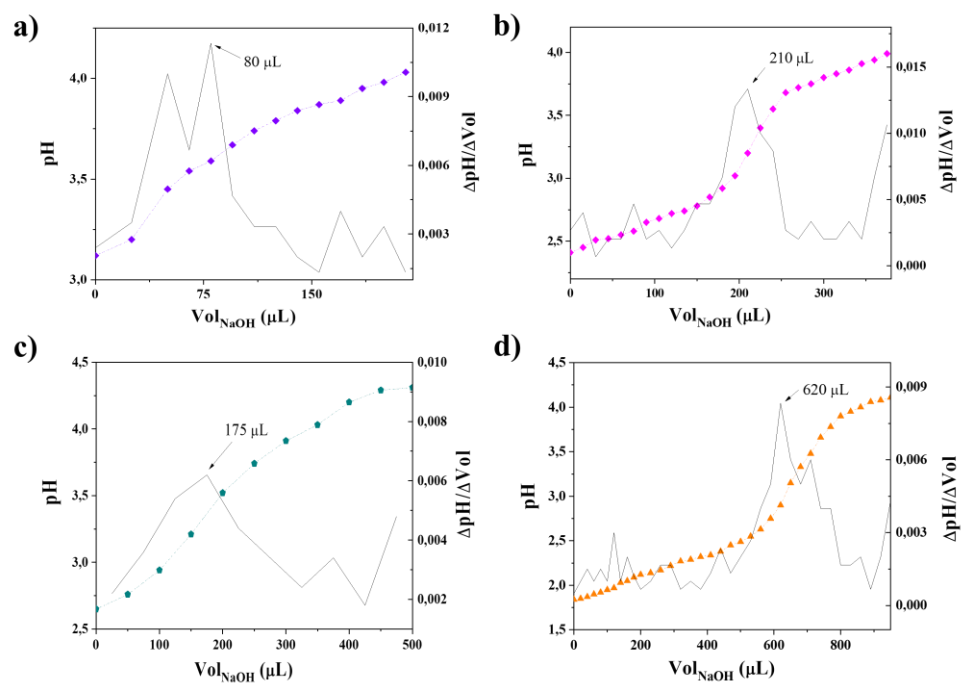
**Fig. SI-1.-** Size exclusion chromatograms in  $\text{NaNO}_3$  0.1 M for a) maltodextrin (MD) and ox-MD at 11 %, and b) maltodextrin (MD) and ox-MD at 48 %, using a right-angle light scattering (RALS,  $90^\circ$ ) detector.



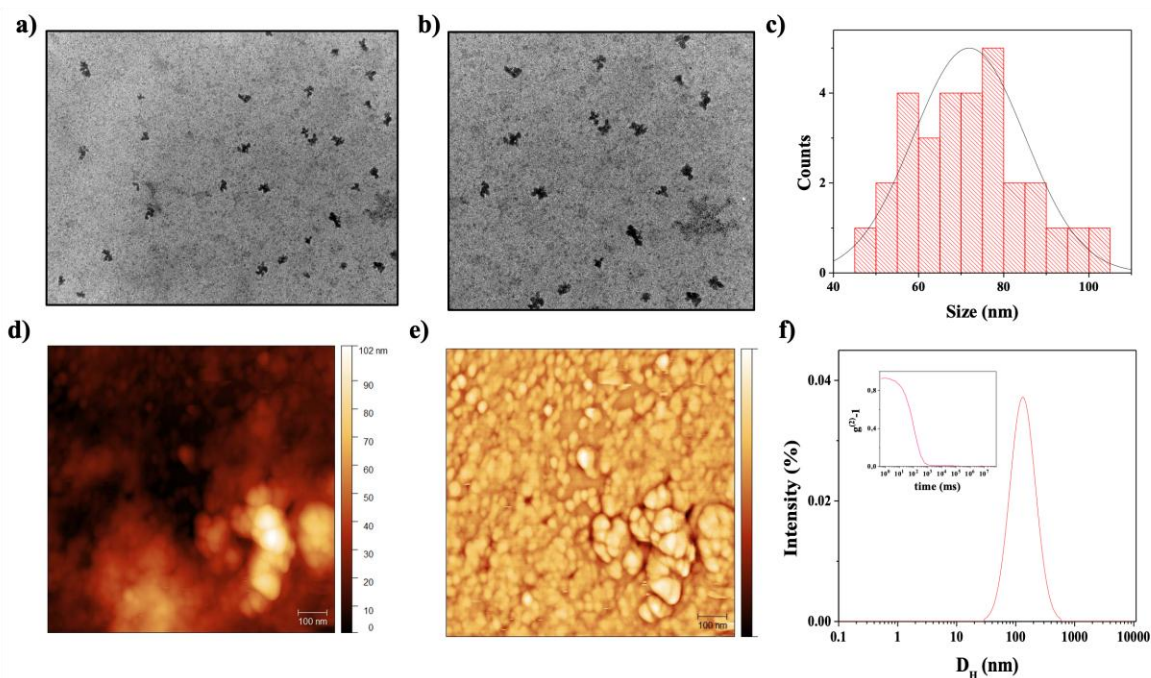
**Fig. SI-2.-**  $^1\text{H}$  NMR spectra, obtained in  $\text{D}_2\text{O}$ ,  $T = 25^\circ\text{C}$ , for a) MD, b) ox-MD at a targeted oxidation degree of 10 % and b) reductive amination product between ox-MD and butylamine.



**Fig. SI-3.**  $^1\text{H}$  NMR spectra, obtained in  $\text{D}_2\text{O}$ ,  $T = 25^\circ\text{C}$ , for a) MD, b) ox-MD at a targeted oxidation degree of 30 % and b) reductive amination product between ox-MD and butylamine.



**Fig. SI-4.-** Potentiometric titrations with their respective first derivative, used to quantify the degree of oxidation of ox-MD with hydroxylamine hydrochloride ( $\text{NH}_2\text{OH}\cdot\text{HCl}$ ) for ox-MD at the following targeted oxidation degrees: a) 10 %, b) 20 %, c) 30 % and d) 50 %.



**Fig. SI-5.-** a) TEM image, b) zoom and c) size distribution determined from the images through ImageJ, for MD/CS nanogels. d) AFM image, e) SEM simulation and f) size distribution, from DLS measurements for MD/CS nanogels. The inset shows the correlation function. MD/CS nanogels were synthesized with CS #1 ( $C_{\text{CS}} = 1 \text{ mg/mL}$ ,  $\text{DA} = 0.30$ ,  $\text{pH} = 5.5$ ) and 48 % ox-MD.

**Table SI-1. Necessary amount of  $\text{NaIO}_4$  to oxidize 2 g of MD in 50 mL of water at different oxidation degrees.**

Maltodextrin sample	Targeted oxidation degree (%)	Maltodextrin amount (g)	$\text{NaIO}_4$ amount (g)
Ox-MD-1	10	2	0.26
Ox-MD-2	20	2	0.52
Ox-MD-3	30	2	0.78
Ox-MD-4	50	2	1.30

### Detailed description of necessary calculations for nanogels synthesis

Firstly, the average molecular weight of the repetitive unit of the chitosan ( $M_o$ , Equation 1) was calculated based on one mol of glucosamine (161 g/mol) and adding 43 g/mol, corresponding to the difference between one mol of N- acetylglucosamine and glucosamine. This difference is only present in the acetylated units of the chitosan, so the degree of acetylation of chitosan (DA) is taken into account in the calculations.

$$M_o = 161 + 43(DA) \quad 1$$

The molar number of amino groups present in the added mass of chitosan (in grams) is calculated in relation to the proportion of glucosamine monomeric units (1-DA) and the average molecular weight of the repeating unit of chitosan (Equation 2).

$$mol NH_2 = \frac{(chitosan\ mass)(1 - DA)}{M_o} \quad 2$$

To know the amount of maltodextrin necessary for each reaction, the amount of aldehyde groups that would be available to act as crosslinking points with the chitosan is taken into account in the calculation. Therefore, the molar proportion of aldehyde groups per mole of maltodextrin was calculated, according to the theoretical percentage of oxidation (Equation 3).

$$mol_{CH=O} / mol_{ox-MD} = \frac{(2)(MW_{ox-MD})(oxydation\ degree)}{(162)} \quad 3$$

In this equation, the molar proportion of CH=O in oxidized maltodextrins ( $mol_{CH=O}/mol_{ox-MD}$ ) is obtained as a function of the molecular weight of the oxidized maltodextrin ( $MW_{ox-MD}$ ), the degree of oxidation and the molecular weight of the monomeric unit present in maltodextrin (162 g/mol).

Finally, the mass (in mg) of oxidized maltodextrin required for each reductive amination reaction was calculated with Equation 4.

$$m_{ox-MD} = \frac{(mol_{NH_2})(eq)(chitosan\ protonation\ \%)(162)}{(oxydation\ degree)(2)(MW_{ox-MD})} \quad 4$$

In this equation, we took into account the amount of moles of available  $\text{NH}_2$ , calculated from *Equation 2*, which depend on the percentage of protonation of chitosan at a given pH (chitosan protonation %). The proportion of  $\text{CH}=\text{O}/\text{NH}_2$  (eq) was varied to adjust the amount of oxidized maltodextrin needed to the amount of sample and to a mass that was experimentally measurable for each reaction.