Injectable self-healing oxidized pectin and carbohydrazide-modified gelatin hydrogels for curcumin-loaded zein nanoparticle delivery in antioxidant therapy

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PDA_10 and PDA_25 synthesis and characterizations

Pectin was oxidized to theoretical degrees of 10 and 25% by adding 128.4 mg and 321 mg of $NaIO_4$ per gram of pectin, with reaction times of 3 and 6 h, respectively. PDA yields of production for PDA oxidized at 10 and 25% theoretical oxidation degrees were measured as 67 ± 10% and 70 ± 9% for PDA_10 and PDA_25, respectively. PDA real degree of oxidation was determined through TNBS assay, by the direct reaction of PDA aldehyde groups with tert-Butyl carbazate (t-BC). Real oxidation degree values were estimated to be 17 ± 0.7 for PDA_10 and 30 ± 0.8 for PDA_25 (**Figure S1A**)**.**

A preliminary characterization of PDA_10 and PDA_25 was performed through ATR-FTIR analysis (**Figure S1B**). Then, the viscosimetric molecular weight (M_v) was analyzed at concentrations of 0.2-0.3-0.4-0.5 % w/v for PDA_10 and 0.4-0.6-0.8-1 % w/v for PDA_25. M_v of PDAs was measured as 27 ± 1.4 kDa for PDA_10 and 16 ± 3 kDa for PDA_25 (**Figure S1C**).

Finally, since oxidation reduces the ability of PDA to crosslink with calcium ions, PDAs hydrogels (4 % w/v concentration) were crosslinked with $CaCl_2$ 100 mM for 10 minutes. However, PDA_10 and PDA_25 hydrogels were not able to crosslink with Ca^{2+} ions and therefore not subjected to further characterization.

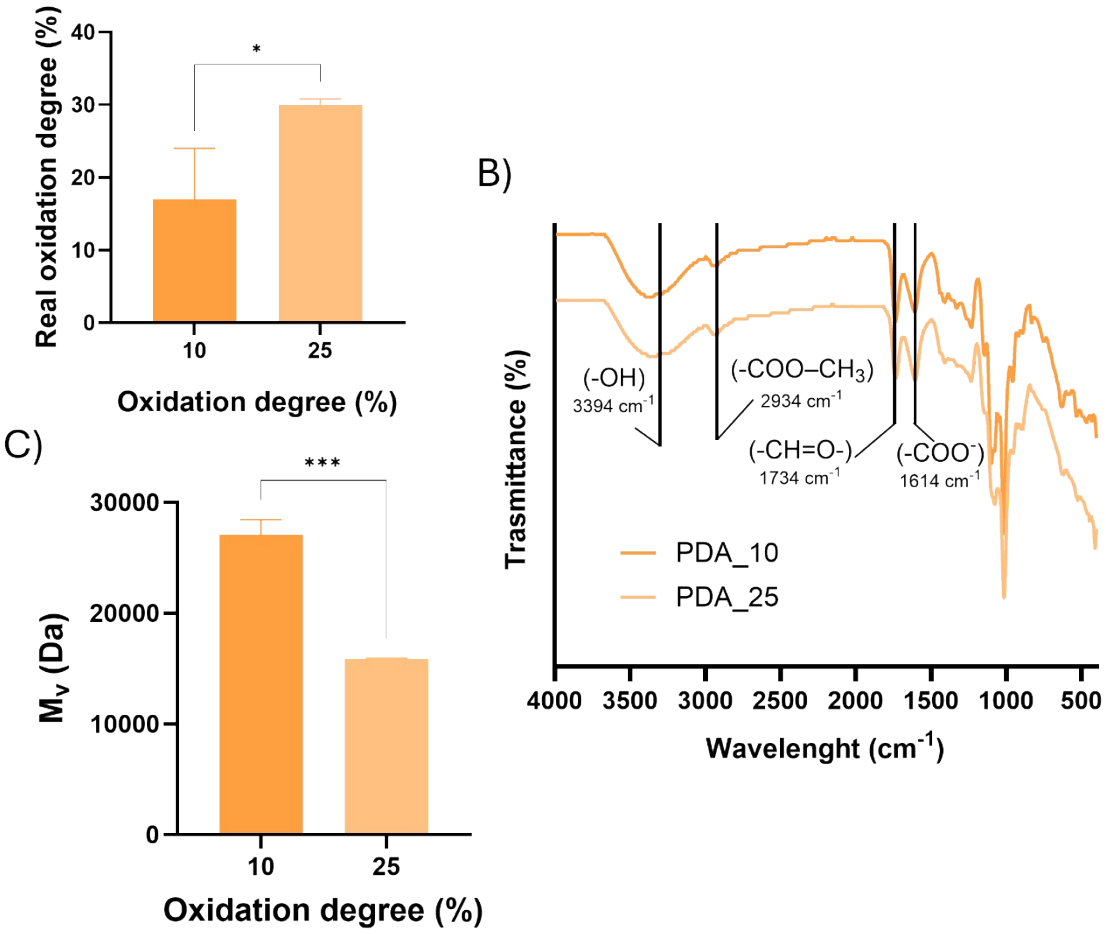

Figure S1. A) Aldehydic content of PDAs (%mol of aldeheyde/mol of galacturonic acid), B) FTIR spectra of PDA_10 and PDA_25, C) Viscosimetric molecular weight of PDA_10 and PDA_25, as a function of theoretical oxidation degree.

PDA/gelatin hydrogel evaluations

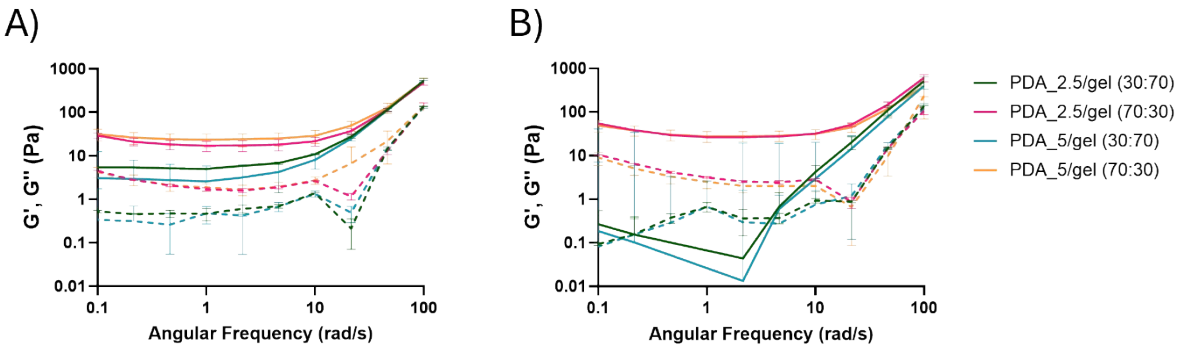

Figure S2. Storage modulus (G', continuous line) and loss modulus (G", dotted line) as a function of angular frequency (1 and 100 rad/s) of PDA (pre-crosslinked with 30 mM $CaCO_3$)/gelatin hydrogels at different PDA:gelatin ratios 30:70 and 70:30% w/w at A) 25°C and B) 37°C.

DLS analyses of CurZNPs release from PDA/G-CDH hydrogels

Table S1. Size measurements by DLS analysis of CurZNPs released from PDA_2.5/G-CDH (70:30) and PDA_5/G-CDH (50:50) hydrogels at the selected time points.

Time points (days)	Size (nm)	
	PDA_2.5/G-CDH (70:30)	PDA_5/G-CDH
1	212±11	230±7
2	212±20	215±3
3	205±29	216±10
7	232±26	208±33
10	209±26	216±16
14	218±35	204±27
21	203±16	210±35
28	255±30	268±23

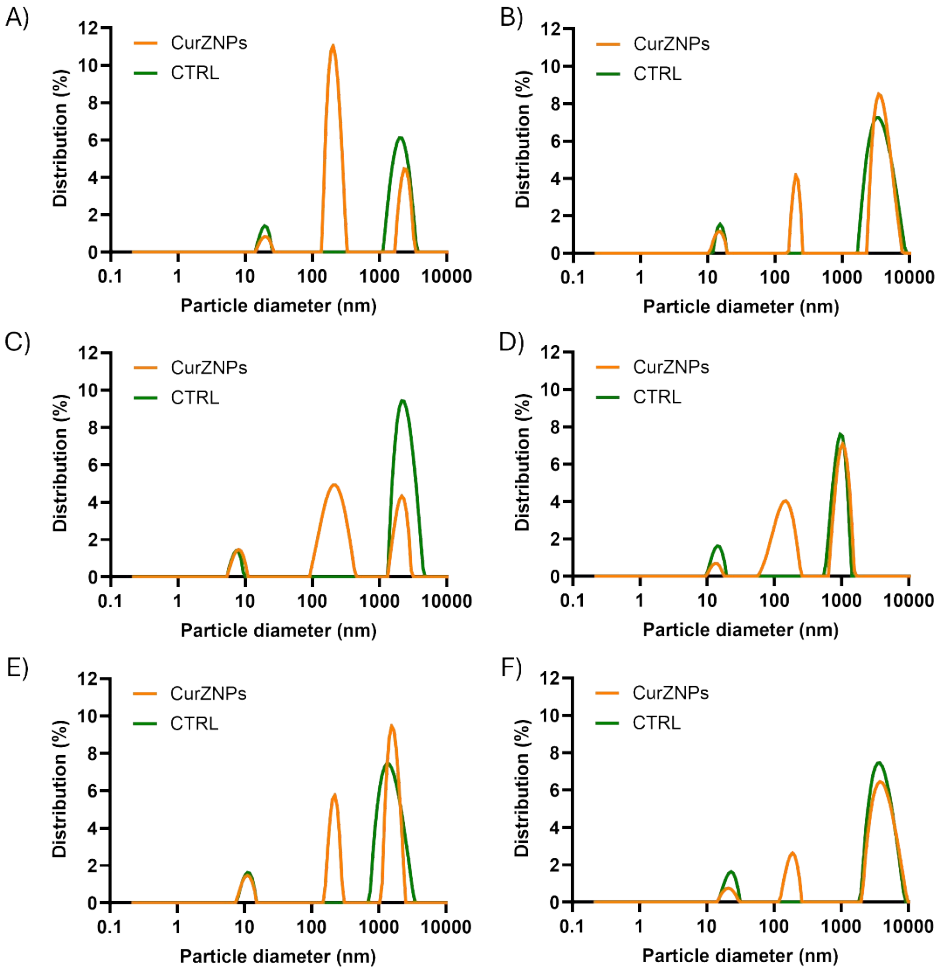

Figure S3. DLS analysis to detect CurZNPs release from A-C-E) PDA_2.5/G-CDH (70:30) where CurZNPs (orange) and CTRL (green) and from B-D-F) PDA_5/G-CDH (50:50) where CurZNPs (orange) and CTRL (green). Reported DLS images are illustrative of single measurements at specific time points of release: A-B) 1, C-D) 3 and E-F) 7 days. It is possible to see that CTRL hydrogels showed two peaks at low and high nm, probably due to hydrogels degradation, while CurZNPs loaded PDA/G-CDH hydrogels exhibit an addictional peak at around 200 nm, suggesting that CurZNPs are released.