Novel Chitosan Based pH-Sensitive and Disintegratable Polyelectrolyte Nanogels



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Introduction

Polyelectrolyte nanogels, which are readily formed by electrostatic inter-action between opposite charged polyelectrolytes, have attracted great inte-rests due to its unique properties, especially for preparation of stimuli-res-ponsive nanogels that responds faster than its macroscopic counterparts to exter-nal stimuli such as pH, temperature, UV/visible light, electrical or combin-ations thereof.

In this work, a novel approach to design pH-sensitive polyelectrolyte nanogels formed by chitosan was reported. It was found that the incorpor-ation of chargereversible citraconic-based chitosan into polyelectrolyte complexes provided an approach to the formation of polyelectrolyte nano-gels that were stable at neutral pH but disintegrated quickly in acidic media.



Fig. 2. Fluorescamine assay of (A) polyanion 1 incubated in PBS or acetate buffer with a concentration of 10 mM at 4 $^{\circ}$ C, 25 $^{\circ}$ C and 37 $^{\circ}$ C; (B) polyanion 1 and 2 incubated in PBS or acetate buffer with different concentrations at 37 $^{\circ}$ C.

3. Preparation and characterization of polyelectrolyte nanogels



Experimental





Fig. 3. (A) Colloid titration assay of different polyelectrolyte pairs in PBS (7.4, 10 mM). (B) D_h and (C) ζ -potential of polyelectrolyte nanogels formed by polycation 2 and polyanion 2. (D) TEM image of the polyelectrolyte nanogels ($V_{add} / V_{SP} = 40\%$)



MVCS	560362	1.475	80%
DCS	22838	1.899	90%
COS	8805	1.092	90%

^a M_n and PDI were measured by SEC. ^b Degree of deacetylation of chitosan.

Results

1. Synthesis and characterization of chitosan-based polyelectrolytes

(A)



Fig. 4. Stability of polyelectrolyte nanogels formed by polycation **2** and polyanion **2** (($V_{add} / V_{SP} = 40\%$) in PBS (7.4, 10 mM) or acetate buffer (5.0, 10 mM) at 37 °C for a period of 24 hours: D_h (A) and ζ -potential (B); TEM images of polyelectrolyte nanogels formed by polycation **2** and polyanion **2** (($V_{add} / V_{SP} = 40\%$) after dialysis for a period of 24 hours in PBS (7.4, 10 mM) (C) or acetate buffer (5.0, 10 mM) (D) at 37 °C.

Conclusions

In summary, we proposed a novel approach to prepare pH-sensitive and disintegratable polyelectrolyte nanogels by incorporating *N*-(carboxyacyl) citraconic-based chitosan with charge-reversible property. The hydrolysis of citraconic-based chitosan was investigated and an isomerism-caused selective hydrolysis was found. The gelatinization of opposite charged chitosan-based polyelectrolytes was evaluated. Results showed that nanogels could be formed only by polyelectrolytes with a very large difference in molecular weight. The incorporation of charge-reversible polyanion into nanogels provided an approach to the formation of polyelectrolyte nanogels that were stable at neutral pH but disintegrated immediately in an hour in acidic media. It is believed that this extraordinary pH-sensitive polyelectrolyte nanogels may have a very promising future in biomedical and biological applications.

Fig. 1. ¹H NMR spectra of (A) polycation **2** and (B) polyanion **1**.

Table 2. The ratio of Proximal to Distal in polyanion 1.

Feed ratio _	Degree of substitution (DS)			
	Total	Proximal	Distal	Proximal:Distal
0.5:1	44.8%	24.5%	20.3%	0.55:0.45
1:1	44.8%	22.7%	22.1%	0.51:0.49
2:1	73.4%	38.6%	34.8%	0.53:0.47
3:1	81.1%	42.7%	38.4%	0.53:0.47
5:1	90.0%*	49.7%	40.3%	0.56:0.44
7:1	90.0%*	50.0%	40.0%	0.51:0.49
10:1	90.0%*	45.7%	44.3%	0.51:0.49

*The integral area of $C_2(H)$ in chitosan at $\delta = 2.66$ ppm is zero

<u>2. Hydrolysis kinetics of polyanions</u>

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