Supporting Information

Degradation behaviors of poly(L-lactic acid) microspheres

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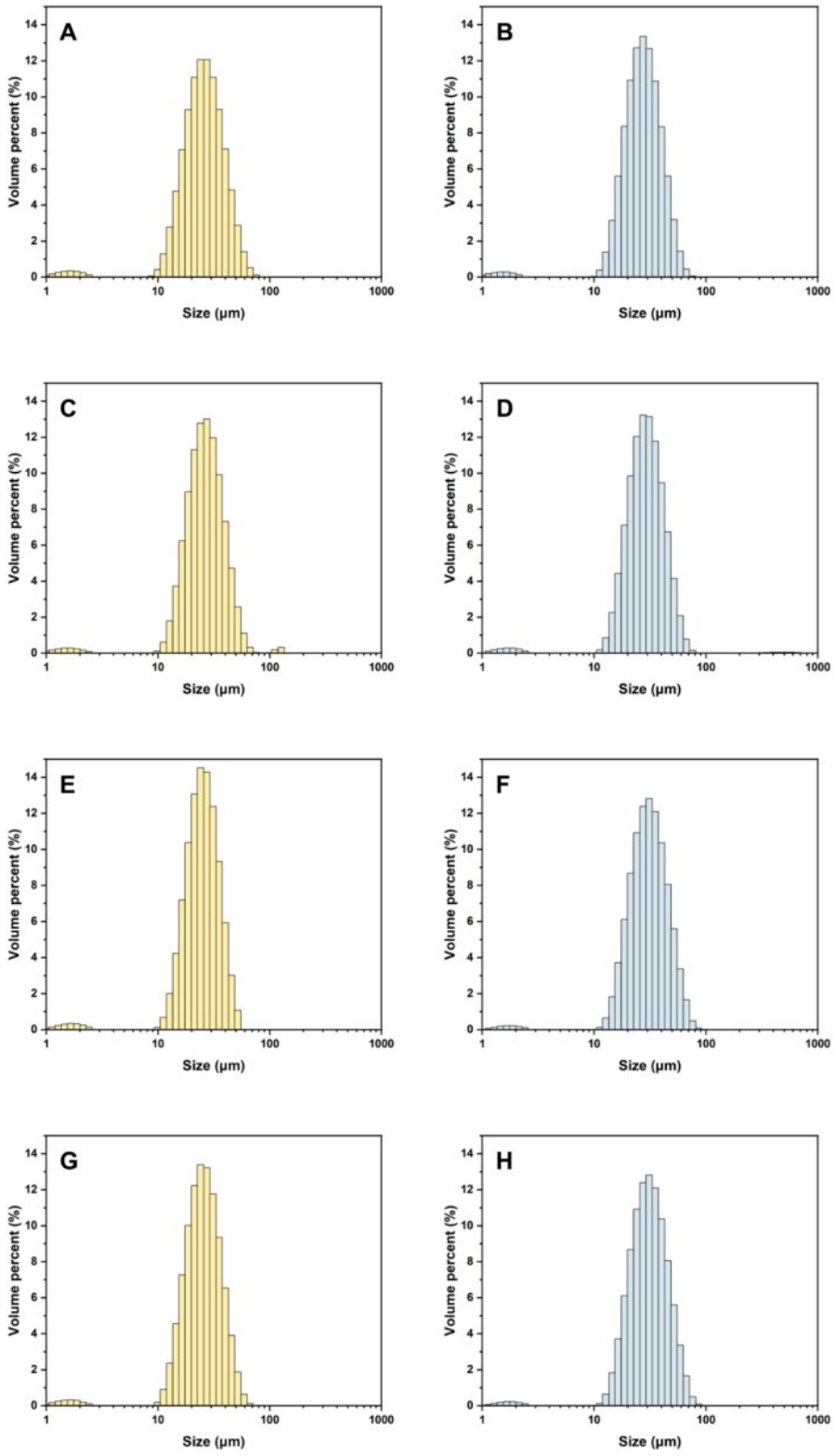


Figure S1. Size distributions of PLLA (A) and PELA (B) microspheres before and after 45-day degradation: PLLA in PBS (C), PELA in PBS (D), PLLA in PBS with proteinase K(E), PELA in PBS with Proteinase K(F), PLLA in PBS with lipase (G), and PELA in PBS with Lipase (H).

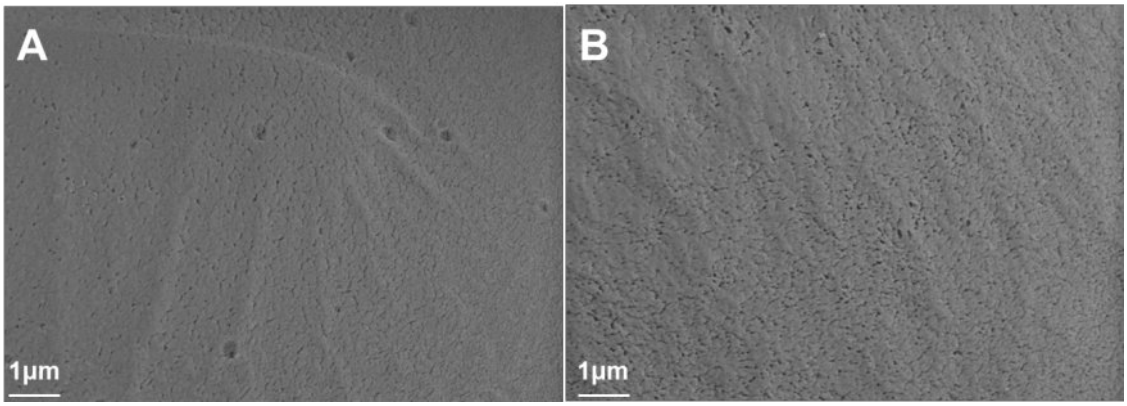
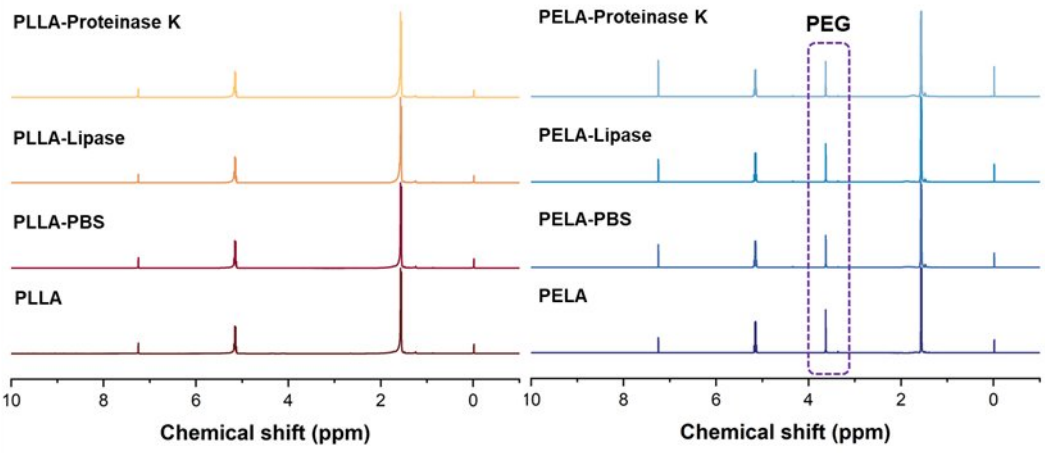


Figure S2. SEM images of the surface of freshly prepared PLLA (A) and PELA (B) microspheres.



(A) (B)

Figure S3. ^{1}H NMR spectrum of PLLA (A) and PELA (B) microspheres before and after degradation in PBS, PBS with Lipase and PBS with Proteinase K.

Table S1. Characteristics of microspheres

Sample	PLLA	PELA
M_n (kg/mol)	33	36
$M_n^{corrected}$ (kg/mol)[a]	19	21
Span[b]	1.04	0.99
Average size (μm)	25	27

[a] The corrected molecular weight is calculated as $M_n^{corrected} = 0.58 \times M_n$[1]
[b] The span value is calculated as follows:

$$Span = \frac{D_{v,90\%} - D_{v,10\%}}{D_{v,50\%}}$$

here $D_{v,90\%}$, $D_{v,10\%}$ and $D_{v,50\%}$ are the volume size diameters at 90%, 50% and 10% cumulative volumes, respectively.

Table S2. PEG content of PELA microspheres [a]

Sample	PEG Content (%)
Before incubation	25
PBS	19
PBS with Proteinase K	20
PBS with Lipase	20

[a] Determined by the ^{1}H NMR spectra in Figure S3.

Table S3. Study of PLA containing microspheres degradation in literature

literature	Composition	microsphere size	PEG content	Enzyme	Degradation condition
This work	poly-(L-lactide)-*b*-poly(ethylene glycol)/ poly-(L-lactide)	~25 μm	25%	Lipase Proteinase	PBS, pH=7.4, 37℃
[2] Li, X.; Deng, X.; Yuan, M.; Xiong, C.; Huang, Z.; Zhang, Y.; Jia, W. In vitro degradation and release profiles of poly-DL-lactide-poly(ethylene glycol) microspheres with entrapped proteins. Journal of Applied Polymer Science 2000, 78 (1), 140-148	poly-(D,L-lactide)-*b*-poly(ethylene glycol)/ poly-(D,L-lactide)	1.5 - 2 μm	10%	none	PBS, pH=7.4, 37℃
[3] Gonzalez, M. F.; Ruseckaite, R. A.; Cuadrado, T. R. Structural changes of polylactic-acid (PLA) microspheres under hydrolytic degradation. *Journal of Applied Polymer Science* **1999**, *71* (8), 1223-1230.	poly-(D,L-lactide)	~20 μm	none	none	Titrisol, pH=7, 37℃
[4] Dorati, R.; Genta, I.; Colonna, C.; Modena, T.; Pavanetto, F.; Perugini, P.; Conti, B. Investigation of the degradation behaviour of poly(ethylene glycol-co-d,l-lactide) copolymer. *Polymer Degradation and Stability* **2007**, *92* (9), 1660-1668.	poly(ethylene glycol-co-D,L-lactide)	~40 μm	10%	none	PBS, pH=7.4, 37℃
[5] Shi, X.; Jiang, J.; Sun, L.; Gan, Z. Hydrolysis and biomineralization of porous PLA microspheres and their influence on cell growth. *Colloids and Surfaces B: Biointerfaces* **2011**, *85* (1), 73-80.	poly-(D,L-lactide) and poly(vinyl alcohol)	~250 μm	none	none	In vivo
[6] Grizzi, I.; Garreau, H.; Li, S.; Vert, M. Hydrolytic degradation of devices based on poly(dl-lactic acid) size-dependence. *Biomaterials* **1995**, *16* (4), 305-311.	poly-(D,L-lactide)	125 - 250 μm	none	none	PBS, pH=7.4, 37℃
[7] Park, T. G. Degradation of poly(d,l-lactic acid) microspheres: effect of molecular weight. *Journal of Controlled Release* **1994**, *30* (2), 161-173.	poly-(D,L-lactide)	~10 μm	none	none	PBS, pH=7.4, 37℃
[8] Blanco, M. D.; Sastre, R. L.; Teijón, C.; Olmo, R.; Teijón, J. M. Degradation behaviour of microspheres prepared by spray-drying poly(d,l-lactide) and poly(d,l-lactide-co-glycolide) polymers.	poly-(D,L-lactide) Poly(D,L-lactide-*co*-glycolide)	~1.3 μm	none	none	PBS, pH=7.4, 37℃
[9] Zolnik, B. S.; Burgess, D. J. Effect of acidic pH on PLGA microsphere degradation and release. *Journal of Controlled Release* **2007**, *122* (3), 338-344.	poly(lactic-co-glycolic acid)	~20 μm	none	none	PBS, pH=7.4 or 2.4, 37℃
[10] Zhou, S.; Deng, X. In vitro degradation characteristics of poly-dl-lactide–poly(ethylene glycol) microspheres containing human serum albumin. *Reactive and Functional Polymers* **2002**, *51* (2), 93-100.	poly-(D,L-lactide)-*b*-poly(ethylene glycol)	~10 μm	10%	none	PBS, pH=5.6, 7.4, and 9.6, 37℃

References

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(3) Gonzalez, M. F.; Ruseckaite, R. A.; Cuadrado, T. R. Structural changes of polylactic-acid (PLA) microspheres under hydrolytic degradation. *Journal of Applied Polymer Science* **1999**, *71* (8), 1223-1230. DOI: 10.1002/(SICI)1097-4628(19990222)71:8<1223::AID-APP2>3.0.CO;2-I (accessed 2025/01/12).

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(7) Park, T. G. Degradation of poly(d,l-lactic acid) microspheres: effect of molecular weight. *Journal of Controlled Release* **1994**, *30* (2), 161-173. DOI: 10.1016/0168-3659(94)90263-1.

(8) Blanco, M. D.; Sastre, R. L.; Teijón, C.; Olmo, R.; Teijón, J. M. Degradation behaviour of microspheres prepared by spray-drying poly(d,l-lactide) and poly(d,l-lactide-co-glycolide) polymers. *International Journal of Pharmaceutics* **2006**, *326* (1), 139-147. DOI: 10.1016/j.ijpharm.2006.07.030.

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(10) Zhou, S.; Deng, X. In vitro degradation characteristics of poly-dl-lactide–poly(ethylene glycol) microspheres containing human serum albumin. *Reactive and Functional Polymers* **2002**, *51* (2), 93-100. DOI: 10.1016/S1381-5148(02)00029-9.