pH-Dependent Degradation of Poly(β-amino ester) Hydrogels

A. Chen and D. A. Puleo
Department of Biomedical Engineering, University of Kentucky, Lexington, KY, USA

Statement of Purpose

Poly(β-amino esters) (PBAEs) are a class of hydrogels that are of interest as degradable cell scaffolding and drug delivery materials. These polymers have material properties and degradation periods that are tunable through their macromer synthesis procedure. Although the degradation profiles of many PBAEs have been observed in previous studies[1,2], the solutions used have typically been phosphate-buffered saline (PBS) of pH 7.4 to model hydrolytic degradation within the human body. While PBS is a common solution that is isotonic with the physiological fluids, it is likely not representative of the conditions found post implantation. For example, the pH of the local environment can decrease to as low as pH 5 during healing processes. Even though this decrease is temporary, the altered chemical environment may affect the degradation profile of PBAEs. Because hydrolysis is an acid-catalyzed process, it may be possible to use low pH solutions to accelerate testing of polyesters. The purpose of the present study was to evaluate the effect of decreased pH on PBAE degradation to better predict the lifespan of implanted PBAEs, as well as enable accelerated testing protocols to be used with longer lasting polymers that would otherwise take prohibitively long to observe.

Methods

A6 and AH6 hydrogels were prepared in accordance with previous studies[2], punched into 1 mm thick by 9 mm diameter discs, and immersed in 2 ml of PBS of varying pH, as adjusted by HCl and NaOH titration. Macromers were synthesized from diethylene glycol diacrylate ("A"), polyethylene glycol diacrylate ("H"), and isobutylamine ("6"). The molar ratio of A:H in the AH6 macromer was 3:1. Macromers were polymerized via UV-initiated free radical photopolymerization using 1 w/w% 2,2-dimethoxy-2-phenyl acetophenone as initiator.

A nondestructive prospective study was performed in which samples incubated at 37ºC in solutions of different pH were periodically dried with Kimwipes, weighed, and placed back into solution until they were no longer coherent. Additionally, AH6 samples were examined over the course of 10 days with daily timepoints, while A6 samples were studied over 72 days with timepoints every 4 days in a destructive degradation study. At each time point, all samples that were not removed for lyophilization received a solution change to avoid saturation of degradation products.

Results and Discussion

Significant differences between degradation profiles were observed for PBAE samples incubated at decreased pH. As shown in Figure 1, A6 degraded at least 33% faster at pH 6.5 and below compared to those in neutral solutions. Similarly, AH6 degraded 27-40% faster in solutions with lowered pH compared to samples at physiological pH (Figure 2). Samples in both groups also displayed altered degradation profiles though earlier and lower peak swelling compared to samples in physiological pH.

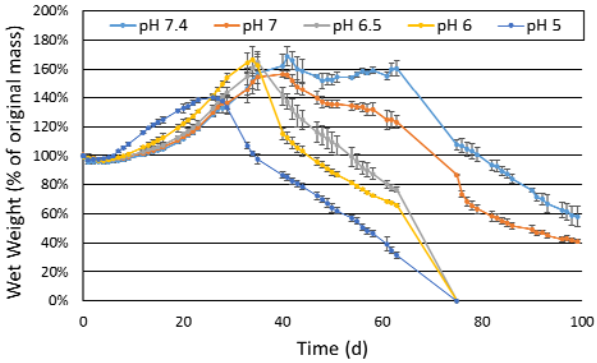

Figure 1. Degradation of A6 samples incubated at different pH.

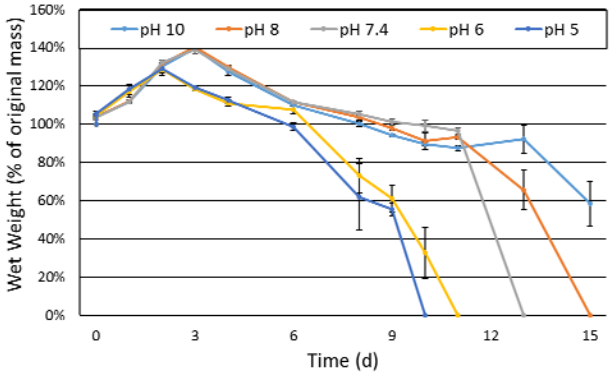

Figure 2. Degradation of AH6 samples incubated at different pH.

Conclusions

The present study indicates that pH had a clear influence on the rate of degradation of A6 and AH6 PBAEs. Elevated pH did not seem to accelerate degradation, but decreased pH caused samples to finish swelling at lower ratios and erode significantly earlier than at physiological pH. The data collected here may be useful for future accelerated degradation studies using A6 or similar slowly degrading materials to extrapolate data to physiological pH.

References

1. Anderson DG et al. Adv Mater. 2006;18:2614-2618.
2. Hawkins AM et al. Polymer 2013;54:4422-4426.

Acknowledgement

This research was funded in part by the NIH (AR060964 and EB017902).