ENZYMATIC, OXIDATIVE AND HYDROLYTIC DEGRADATION OF P(LA-b-TMC) COPOLYMERS

AGNIESZKA ADAMUS-WŁODARCZYK[1]*, MARTA SOCKA[2], RADOSŁAW WACH[1], BOŻENA ROKITA[1], PIOTR ULAŃSKI[1]

[1] INSTITUTE OF APPLIED RADIATION CHEMISTRY, FACULTY OF CHEMISTRY, LODZ UNIVERSITY OF TECHNOLOGY, WROBLEWSKIEGO 15, 93-590 LODZ, POLAND
[2] DEPARTMENT OF POLYMER CHEMISTRY, CENTRE OF MOLECULAR AND MACROMOLECULAR STUDIES, POLISH ACADEMY OF SCIENCES, SIENKIEWICZA 112, 90-363 LODZ, POLAND
*E-MAIL: AGNIESZKA.ADAMUS@P.LODZ.PL

[ENGINEERING OF BIOMATERIALS 153 (2019) 65]

Introduction

Polylactide (PLA) is a well-known polymer that has been studied extensively for various biomedical applications due to its acceptable biocompatibility, inherent biodegradability, high modulus, and strength. Nevertheless, the high crystallinity of PLA results in poor elasticity and long resorption time of 2-3 years [1]. Poly(trimethylene carbonate) (PTMC) seems to be a perfect candidate to introduce elasticity to rigid PLA through blending or copolymerization; it is a rubbery and flexible material [2]. Copolymerization is a typical method of tailoring polymeric biomaterials properties because the specific architecture and composition of the copolymer can be easily obtained. Therefore, combined properties of a rigid chain from high Tg polyester with soft segments from rubbery polycarbonate can be achieved by introducing PTMC as a soft block into brittle PLA segments [3]. Such modification is also crucial in terms of biodegradation mechanism and kinetics of copolymers. In this work, we have focused on comparison of P(LA-b-TMC) copolymers with lactide (LA) contents of 70% and 50% upon degradation in three distinct environments.

Materials and Methods

P(LA-b-TMC) block copolymers with compositions LA/TMC 50/50 and 70/30 were subjected to enzymatic, oxidative and hydrolytic degradation. As controls, homopolymers of PLA and PTMC were used. Rectangular specimens of 50 mm × 5 mm were incubated at 37°C in pH 7.4 phosphate buffered saline (PBS) or in buffer containing 0.2 mg/ml lipase (refreshed every 3 days). Oxidative degradation was performed in 3% hydrogen peroxide solutions with 60 mM Co^{2+} at 37°C, refreshed once a week. Samples were periodically removed from the incubation solution, washed with deionized water, vacuum dried at room temperature and subsequently investigated by physicochemical methods. Tensile properties testing was complemented by the evaluation of mass loss, water uptake, contact angle, morphology (SEM), molecular weight of polymer (GPC) and thermal properties (DSC). Data are discussed in comparison with ^{1}H NMR results which allowed to follow changes of the composition and average sequence distribution of LA/TMC components.

Results and Discussion

Enzymatic degradation. Lipase is effective for degradation of PTMC-based homo- and copolymers, whereas lactide is resistant to this enzyme – no significant mass loss was detected in neat PLA after 17 weeks. In contrast, the copolymers exhibited various degradation rates. Mass loss of P(LA-b-TMC) 70/30 was slower than that of 50/50 which reached nearly 3% (17 weeks). The highest mass loss (18%) was observed for the PTMC homopolymer. The composition of the copolymers remained almost unchanged during the degradation period. On the other hand, the Mn of the P(LA-b-TMC) copolymers slightly decreased, while that of PTMC remained nearly constant during enzymatic degradation. Enzymatic degradation is a surface erosion process which does not affect the bulk properties yet, the hydrolysis still takes place in the bulk of copolymers.

Hydrolytic degradation. PTMC homopolymer degrades extremely slowly as no mass loss was detected. In contrast, P(LA-b-TMC) copolymers appear degradable through hydrolysis. No mass loss was observed for P(LA-b-TMC) 70/30 during the first 6 months, while the mass loss of P(LA-b-TMC) 50/50 decreased 3% after only 2 months. Hydrolytic cleavage, of, as presumed, ester linkages in copolymer chains, starts immediately after immersion in PBS, leading to rapid Mn decrease. Nevertheless, significant mass loss is observed much later, i.e., beyond 6 months. Mn of the copolymers significantly decreased, from c.a. 20 to 6 kDa, from 6 months to 12 months. The degradation products, i.e. low molecular weight species are thus formed and released into the medium, which resulted in rapid mass loss. LA units are preferentially degraded along the copolymer chains, leading to compositional changes.

Oxidative degradation. During the first 5 weeks all samples exhibited negligible weight loss < 0.5% and also small degradation rate based on the GPC results. Thereafter, the degradation rate becomes different for samples with various LA contents. For PLA and samples of LA/TMC molar ratio 70/30 a small weight loss below 1.0% is detected at 15 weeks. In the case of P(LA-b-TMC) 50/50 and PTMC, apparent weight loss is detected from 10 weeks, 2.0% and steadily increases to 5.0% at 15 weeks. In contrast to the weight loss, the molecular weight of PTMC sample and P(LA-b-TMC) 50/50 remained constant for 10 weeks; further a slight decrease in Mn was observed. In the case of PLA and P(LA-b-TMC) 70/30 a substantial drop in molecular weight was observed after 5 weeks, which was reflected also in the mechanical properties of the studied materials.

Upon degradation in all types of media, PLA and P(LA-b-TMC) 70/30 became brittle and eventually fell apart. PTMC and P(LA-b-TMC) 50/50 samples deformed – attained globular shape, became soft and adhered to the incubation vessel wall. In the course of degradation, the surfaces of those two samples became rough and a highly hollow structure was detected after 5 weeks, the size and depth of the hollows increased with the incubation time.

Conclusions

In this study, we have demonstrated that homopolymers and their copolymers degrade differently, depending on their morphological and chemical composition and the nature of incubation medium. Given this knowledge, we are able to tailor not only mechanical properties but also degradation characteristics by combining PLA backbones with TMC segments. The toolbox of techniques that has been used to study the degradation of biomaterials can be applied and employed to select biomaterials that are going to be used for pre-clinical in vivo studies with regard to a variety of clinical applications.

Acknowledgments

This study was funded by the National Science Center, Poland, grant No. 2012/05/N/ST5/01869.

References

[1] Slomkowski S, Penczek S, Duda A., Polym Adv Technol. 25 (2014) 436-447.
[2] Zhang Z, Kuijer R, et. al., Biomaterials 27 (2006) 1741-1748.
[3] Socka M, Duda A, et al., Polymer 87 (2026) 50–63.