

Engineering the Rate of Degradation of Polyester Scaffolds for Bone Tissue Engineering

Kirsten N. Cicotte^{1,2}, Shawn M. Dirk¹ and Elizabeth L. Hedberg-Dirk^{2,3}

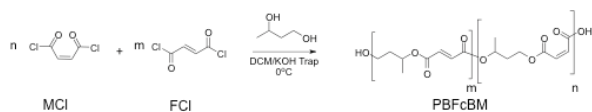
¹ Organic Materials Department, Sandia National Laboratories, Albuquerque, NM

² Center for Biomedical Engineering, University of New Mexico, Albuquerque, NM

³ Department for Chemical and Nuclear Engineering, University of New Mexico, Albuquerque, NM

Statement of Purpose: Recently, the synthetic polymer poly(propylene fumarate) (PPF) has shown promise in orthopedic tissue engineering due to its biodegradability, biodegradability, and ease of processing.¹ Although PPF-based scaffolds have enabled *in vivo* generation of new bone, the rate of scaffold degradation is insufficient to allow for proper bone growth.² The work presented herein builds on the exploration of synthetic routes to polymerize the homopolymer of poly(butylene fumarate) (PBF) and the copolymer poly(butylene fumarate)-*co*-(butylene maleate) (PBFcBM) with controlled fumarate to maleate ratios (F:M). We hypothesize that the crosslinked network degradation will vary with the maleate content (%M).

Methods: Polymer Synthesis. Copolymers of PBFcBM were synthesized from stoichiometric ratios of maleoyl chloride (MCl) and fumaryl chloride (FCI) with butylene diol (BD) following an established procedure (Scheme 1). Copolymers were synthesized with various F:M ratio of 75:25, 50:50 and 25:75. Homopolymers of PPF and PBF were also synthesized under the same conditions using FCl and propylene diol (PD) or BD.



Scheme 1. Synthesis of PBFcBM from MCl and FCI

Polymer Characterization. Upon successful synthesis of all PBFcBM compositions, the F:M ratio was verified using ¹H Nuclear Magnetic Resonance (NMR) and Fourier Transform Infrared Spectroscopy (FT-IR). Other general characterization included determination of molecular weight, glass transition temperature, polymer density before and after crosslinking as well as M:F ratio before and after crosslinking. **Polymer Crosslinking.** A 3wt% phenylbis(2,4,6-trimethylbenzoyl)-phosphine oxide (BAPO)/ gram polymer solution was prepared and crosslinked by UV at 365 nm. **Degradation:** A polymer/BAPO (3wt%) solution was poured into glass vials (diameter = 6 mm) with centrifugation (3 min at 5000rpm). Polymer samples were partially crosslinked at $\lambda = 365$ nm (~1 min) using a UV Fusion®. Vials were broken and polymer removed with continued crosslinking (~5 min). Samples were cut to a height of 12 mm. Samples were subjected to accelerated conditions (0.1N NaOH, 60°C, 65 rpm) for 0, 24, 36 and 48 hours followed by compressive moduli and mass loss analysis.

Results: We have developed and verified a synthetic route to control the F:M ratios in PBFcBM polymers. Integration of the fumarate and maleate olefin peaks (NMR) as well as determining the %M and %F from the

extinction coefficient (FTIR) confirmed successful synthesis of all PBFcBM ratios (data not shown). FTIR was used to verify conservation of F:M ratios in crosslinked networks. The spectral trend for the F and M (Figure 1A) as well as the F:M ratio as a function of UV dose (Figure 1B) confirm no change in ratio upon crosslinking. Evaluation of maleate content effect on degradation was compared to the all fumarate based PPF and PBF networks, where 50:50 PBFcBM showed an increased mass loss over both PPF and PBF (Figure 2).

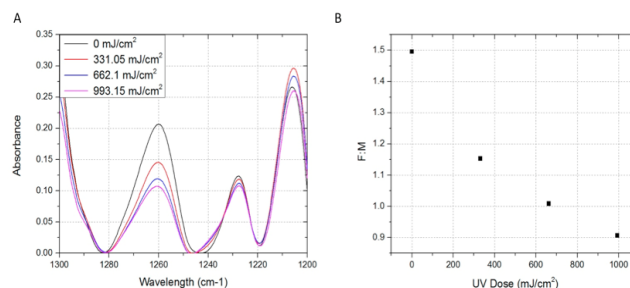


Figure 1. (A) FTIR absorption spectra for PBFcBM. The olefin peaks ~ 1260 cm⁻¹ (fumarate) and ~ 1230 cm⁻¹ (maleate) broaden as a function of crosslinking, keeping the same general peak shape. (b) Corresponding F:M ratio calculated using the extinction coefficient FTIR method (B).

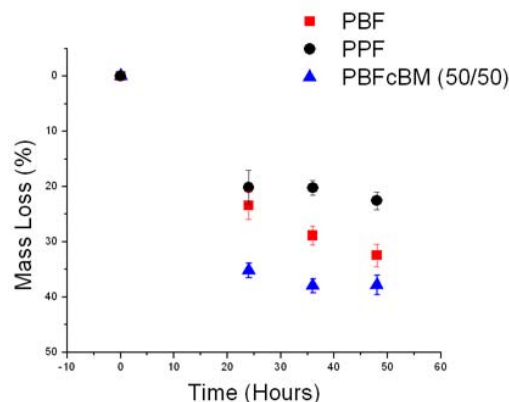


Figure 2. Mass loss of PPF, PBF and PBFcBM (5:50) under accelerated degradation conditions.

Conclusions: We have developed a synthetic route to successfully control to F:M ratio in the PBFcBM copolymer system and, more generally, any fumarate and maleate-based polyester system. In addition FTIR confirms no isomerization from maleate to fumarate upon crosslinking, conserving the initial F:M ratio. Degradation studies support our hypothesis, with an increase in mass loss with polymers containing maleate over the all fumarate polyesters.

References: (1) Hedberg EL *et al* (2005) *Biomaterials* 26 4616-23