

Tailoring Polymer Degradation through Engineering of the Chemical Structure

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Statement of Purpose: The widely studied synthetic polymer poly(propylene fumarate) (PPF) has shown promise in orthopedic tissue engineering. Although PPF-based scaffolds have enabled *in vivo* tissue formation, the rate of scaffold degradation is insufficient to allow for proper bone growth.¹ Recently our laboratory has focused on tuning the rate of polymer degradation through systematic modification of the backbone. The work presented here examines the effect of an added methylene unit (-CH₂) between the crosslinkable carbon-carbon double bonds (C=C) to form poly(butylene fumarate) (PBF). We hypothesized that the increased distance between crosslinkable groups would increase crosslinking efficiency while increasing ester hydrolysis and degradation of PBF relative to PPF.

Methods: Polymer Synthesis. Polymer synthesis of PPF and PBF was carried out as previously described.² Briefly, ring opening polymerization (ROP) of maleic anhydride (MA) and 1,2-propylene glycol (PG) or 1,3-butylene glycol (BG) was carried out at high temperatures PPF and PBF with similar molecular weights (1851 and 2213, respectively). **Polymer Crosslinking.** A 3wt% phenylbis(2,4,6-trimethylbenzoyl)-phosphine oxide (BAPO)/ gram polymer solution was prepared and crosslinked by UV at 365 nm. **Network Characterization.** Crosslinked PPF and PBF networks were evaluated to determine crosslinking efficiency. Reduction in the C=C bond with crosslinking was carried out by differential scanning calorimetry (DSC) and fourier-transform infrared spectroscopy (FT-IR). Relative size of the degradation products were examined via high-performance liquid chromatography (HPLC)⁴, evaluating the degradation products of the crosslinked polymer relative to uncrosslinked material. **Degradation:** A polymer/BAPO (3wt%) solution was poured into glass vials (d=6 mm). Polymer samples were partially crosslinked at $\lambda = 365$ nm (~1 min) using a UV Fusion®. Samples were removed from molds, further exposed to UV (~5 min), and cut to a height of 12 mm. Network degradation was conducted under accelerated conditions (0.1N NaOH, 60°C, 65 rpm) and examined through compressive modulus and dimensional changes.

Results: We have developed and verified a novel synthetic route to prepare PBF and PPF from an acid catalyzed ROP of MA with their respective diol. Characterization of crosslinked networks was performed using various techniques. DSC was used to measure heat capacities (Cp), which change with crosslinking due to reduction in the in polymer degrees of freedom. This method yielded crosslinking efficiencies of 84 and 94% for PPF and PBF. Direct measurement of double bonds was done through FT-IR, yielding similar efficiencies of

85 ± 3 and 98 ± 2%. Evaluation of degradation products by HPLC corroborated the efficiency trends of PPF and PBF at 76 ± 3 and 87 ± 2%. Despite greater crosslinking efficiency, PBF had increased water adsorption compared to PPF (**Figure 1**) both initially and over time. Increased water ingress into the polymer network led to a greater rate of ester hydrolysis.

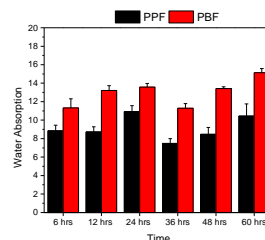


Figure 2. Water absorption, or % water uptake for PBF (repeat unit = 13) as compared to PPF (repeat unit = 12) up to 60 hrs under accelerated degradation conditions (n = 5).

Compressive modulus, and changes in mass were measured as an indicator of degradation (**Figure 2**).

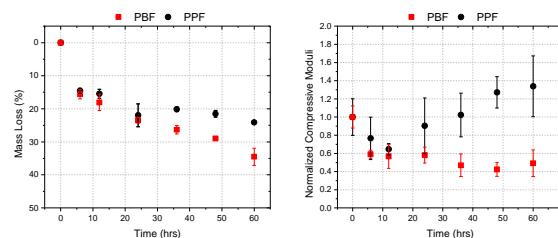


Figure 1. Percent mass loss (left) and normalized compressive moduli (right) for PBF (■) as compared to PPF (●) up to 60 hrs (n=5) under accelerated degradation conditions.

Both PPF and PBF lost mass in the first 24 hrs. Thereafter, PBF continued to lose mass whereas PPF remains unchanged. Compressive moduli of PBF decreased over time, while that of PPF increased. This phenomenon has been attributed to continued crosslinking.⁴

Conclusions: We have synthesized and evaluated the novel fumarate-based PBF that contains an additional methyl group in its repeat unit relative to PPF. Network characterization conducted through multiple techniques demonstrates that the PBF has a high degree of crosslinking than PPF. Despite this, the added methyl groups allowed for increased water ingress, which led to an increased rate of degradation as determined through mass loss and compressive moduli.

References: ¹Hedberg EL *et al* (2005) *Biomats* **26** 4616-23 ²Cicotte KN *et al* (2010) *J of App Polym Sci* **117** (4), 1984-1991 ³Timmer MD *et al* *Macromol* (2002) **35**, 4373-4379 ⁴Timmer MD *et al* *Biomats* (2002) **24** (4), 571-577