Polymer Bulletin 31, 331–338 (1993)

Polymer Bulletin

Poly(glycolic acid) fiber-reinforced bioabsorbable composites with improved interfacial properties

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Abstract

Bioabsorbable composites, designed for use as rigid tissue scaffolds, were fabricated by reinforcing free radically cured poly(D,L-lactide) fumarate matrices with absorbable poly(glycolic acid) fibers. To investigate the benefits of an improved fiber/matrix interphase, fiber pretreatments were employed including surface-etching by exposure to mild acidic conditions and incorporation of 3-methacryloxypropyltrimethoxysilane as a coupling agent. SEM of composite fracture surfaces showed that fiber pretreatment yielded improved wetting and encapsulation of the fibers by the matrix resin. The composites fabricated with poly(glycolic acid) fibers which were acid-etched and pretreated with the coupling agent showed an average 41% increase in tensile strength; a representative sample displayed an increase from 73.9 MPa to 105.5 MPa, compared to the composite made from untreated fibers.

Introduction

The development of biocompatible, load-bearing orthopaedic materials that slowly degrade is an important area of research with numerous potential benefits. High molecular weight, linear poly(glycolic acid), poly(lactic acid) and poly(ε-caprolactone) have proven to be the most useful bioabsorbable polymers since their degradation products are naturally occurring metabolites or are essentially non-toxic. These polymers have therefore been effectively fashioned into a number of surgical/medical devices including sutures, soft or hard tissue scaffolds, and controlled drug delivery matrices.[1-3] However, because these popular medical-grade polymers are, without exception, semi-crystalline thermoplastics, they all tend to hydrolyze initially only in the amorphous regions, and thus the physical properties of the materials decrease dramatically before any significant bioabsorption has taken place. This two-phase morphology, characterized by different degradation rates in the crystalline and amorphous regions, can lead to a dramatic loss in strength before a significant mass loss has occurred. A more linear loss in strength with loss of mass can theoretically be obtained if wholly amorphous polymers are used.[4,5] In fact, Storey and Hickey have reported poly(ester-urethane) networks derived from poly(ε-caprolactone-co-D,L-lactide) or poly(trimethylene carbonate-co-D,L-lactide) polyols crosslinked with toluene diisocyanate, which displayed a linear loss of strength with respect to mass during the first thirty days of degradation. Perhaps the strongest case for amorphous prepolymers and networks, however, is that the fabrication of composites is greatly facilitated. Low viscosity prepolymers more readily wet fiber surfaces and flow into the interstices of reinforcing fibers and fabrics. This wetting allows for the fabrication of a composite with fewer imperfections, leading to a more fully developed interphase.

Totally absorbable composites, which have potential applications as tissue scaffolds and ultimately as absorbable bone plates, can be fabricated by reinforcing bioabsorbable polymer matrices with absorbable fibers. However, bioabsorbable composites have been limited in high-load applications due to insufficient physical properties. The physical properties of a composite can be improved if it is carefully designed at the fiber/matrix interface, which is a crucial region that is responsible for the transference of energy from the matrix into the load-bearing fibers. Application of a coupling agent or pre-treatment of the surface of the fibers is an important design element and will increase the physical properties and fatigue life of the composite.

Poly(glycolic acid) monofilaments or surgical meshes are excellent reinforcements for totally absorbable composites since they are highly oriented along the primary axis of the fibers and display high tensile strengths and moduli. Several matrices are under development for use in the fabrication of absorbable composites, such as poly(ester-urethane)[6], poly(ester-epoxide)[7], poly(ester-methacrylate).[8] To maximize the physical properties of the composite, it is important to minimize the difference in surface energies between the fiber and matrix, thus increasing the wetting and encapsulation of the fibers by the matrix. Treatment of the poly(glycolic acid) fibers with a coupling agent, for example, one containing functional groups which may react with the matrix resin, is necessary to optimize the physical properties of a bioabsorbale composite through improved interfacial wetting.

Experimental

Synthesis of Poly(D,L-lactide) Fumarate:

Unsaturated poly(D,L-lactide) fumarate was synthesized by the following procedure: 200g (1.39 moles) D,L-lactide (Aldrich), 30.6g (0.347 moles) 2-butene-1,4-diol (Aldrich), and 0.077g stannous octoate (Sigma) (0.25 wt% relative to the initiator) were added to a 1000 ml 3-necked round-bottomed flask equipped with a mechanical stirrer and nitrogen purge. The flask was immersed in a 100 °C silicone oil bath for 16 h, at which time NMR and GPC data were obtained.

Based on the theoretical molecular weight (664.6 g/mole), 35.23g (0.400 moles) of fumaric acid (Aldrich) was added to the reactor, the temperature was increased to 160 °C, and the contents were allowed to stir for 16 h. When the reaction mixture cleared, the reactor was removed from the bath and allowed to cool to room temperature. The polymer was then dissolved in $CHCl_3$, precipitated into stirring hexanes, and vacuum dried at 60 °C for 2 days after which the final GPC and NMR analyses were performed.

Formation of Free Radically Cured Networks:

Polymer (~25.0 g) was dissolved in $CHCl_3$ (~25 wt% relative to polymer) to make a stock resin which was pre-promoted with 0.6% cobalt napthenate. The mixture was stirred until homogeneous. 2-Butanone peroxide was used as the free radical initiator. Networks were cured by placing ~5 g of promoted resin and 1.5 wt % initiator (relative to the resin) into an aluminum pan that had been precoated with a mold releasing agent. The contents were stirred by hand with a wooden spatula and placed in a curing oven at 60 °C for 24 h. Next, the pans were placed in a vacuum oven at 60 ^{o}C for 24 h to allow for the final cure of the networks.

Incorporation of Coupling Agent:

Poly(glycolic acid) fibers were surface-etched by exposure to acidic conditions. The fibers were placed in a stirred solution of HCl and water (pH = 3.0) for 15 min, and dried in a vacuum oven for 1 h to remove any excess solution. The resultant fibers possessed hydroxyl and carboxylic acid groups on their surfaces that were further reacted with a functionalized coupling agent.

The coupling agent was deposited onto the fiber surface by placing the acid-etched fibers into a 2% solution of coupling agent in a 95/5 ethanol/water solution that was adjusted to pH 4.5-5.5 with acetic acid. The fibers were immersed in the stirred solution for approximately 10 min. The solution was decanted off, and the fibers were rinsed twice with ethanol to remove any excess solution. Removal of excess ethanol and curing of the coupling agent layer were carried out at 110^{o}C for 10 min in a vacuum oven.

Fabrication of Bioabsorbable Composites:

Composites were fabricated with knitted poly(glycolic acid) fiber-based surgical mesh (DEXON style #8). The fabric was cut into approximately 2 cm x 3 cm samples and saturated with the pre-initiated polyester matrix resin. Laminated plates consisting of four layers of fabric were fabricated using standard vacuum bag molding techniques.[9] These plates were cured for 24 h at room temperature, removed from the vacuum bag, and cured an additional 24 h at 80 ^{o}C.

Characterization:

The matrix resins were characterized by ^{13}C NMR and ^{1}H NMR using a Bruker Model AC-200 (75.48 MHz) spectrometer, and FT-IR using a Bruker Model IFS-88. Molecular weights of the prepolymers were determined by hydroxyl titration with KOH/MeOH (0.498 N) solution;[10] molecular weight distributions of the hydroxy-terminated prepolymers were estimated using a Waters Associates gel permeation chromatograph (GPC) which has been previously described.[11] The extent of wetting and interfacial analysis of the fiber/matrix were analyzed by environmental scanning electron microscopy (ESEM) using an Electro Scan model E-20 microscope. Composite tensile strengths and moduli were determined prior to, and after surface treatment, using an MTS Model 810 Universal Test Machine. Composite samples were cut into rectangular shapes of ~10-12 mm x ~35-40 mm, and thicknesses varied between ~1-3 mm. Five samples of each system were pulled at a strain rate of 0.50 mm/s, and the average tensile properties were reported.

Results and discussion

As shown in Figure 1, the polyester matrix resin was synthesized via ring opening polymerization of D,L-lactide with 2-butene-1,4-diol as initiator and stannous octoate as catalyst. Molecular weight of the hydroxy-terminated prepolymer may be controlled by varying the monomer to initiator feed ratio which was held at 4:1 (mole: mole) in this work. The polymerization was carried out for 16 h at 100 °C, after which time, the hydroxy-terminated prepolymer was chain extended with fumaric acid to yield the unsaturated poly(D,L-lactide) fumarate. This reaction was carried out for 16 h at 160 °C. Unreacted monomer was removed by dissolving the polymer in $CHCl_3$ and reprecipitating twice into stirring hexanes.

Figure 2 shows the GPC chromatograph of the hydroxy-terminated prepolymer, A, and the chain extended prepolymer, B. The increase in molecular weight upon chain extension is reflected in the shift of the molecular weight distribution to shorter times and thus higher molecular weight.

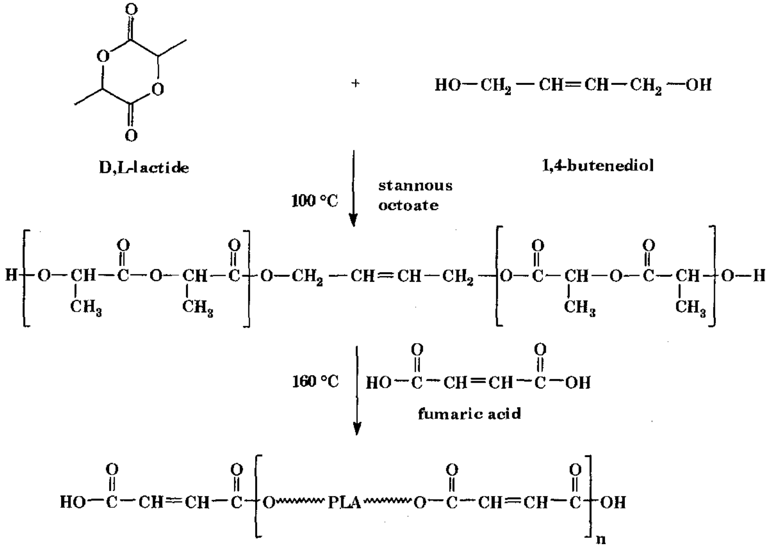

Figure 1: Reaction of D,L-lactide with 1,4-butenediol and chain extension of the initiated oligomer with fumaric acid

^{13}C NMR spectra of the hydroxyl-terminated and the chain extended prepolymer are shown in Figure 3 and 4, respectively. The former prepolymer was of sufficiently low molecular weight to allow easy differentiation among lactide carbons that are located in the main chain, adjacent to an hydroxyl end group, or adjacent to the initiator residue. Main chain carbonyl, methine, and methylene carbons were assigned to the peaks labeled 1b, 3b, and 5b, respectively. The methine and methylene carbons of lactide units adjacent to the end group were assigned to peaks 3a and 5a, respectively; the carbonyl carbon for the lactide unit adjacent to an initiator was assigned to peak 1a. Upon chain extension, the molecular weight increased to the point where the effects of the end groups were no longer pronounced (Figure 4). This was confirmed by the disappearance of peaks associated with the end groups, and the appearance of two new peaks, 6 and 7, which were assigned to the carbonyl and methine carbons, respectively, of the incorporated fumaric acid units.

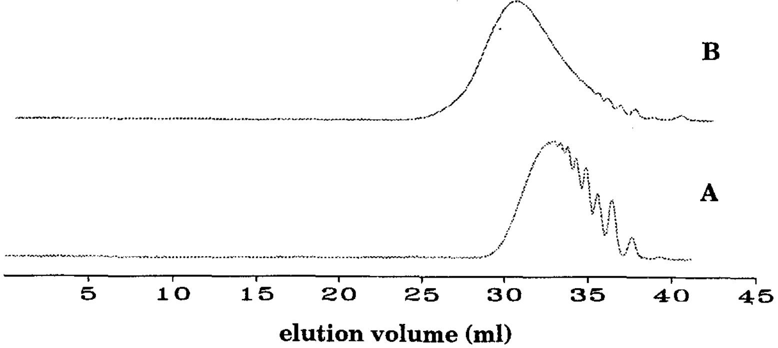

Figure 2: Gel permeation chromatograph (GPC) of poly(D,L-lactide) fumarate: A- initial prepolymer; B- chain extended prepolymer

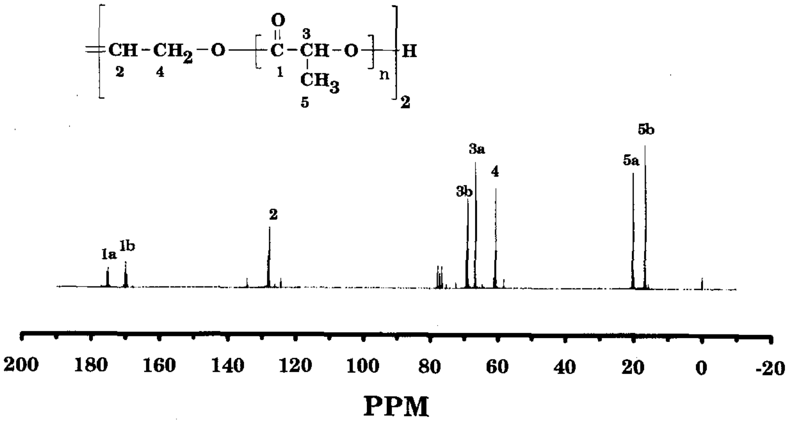

Figure 3: ^{13}C NMR spectrum for poly(D,L-lactide) diol precursor

Bioabsorbable composites were fabricated by reinforcing the poly(D,L-lactide) fumarate networks with treated and untreated poly(glycolic acid) surgical meshes. A primary objective of the research was to observe the increase in physical properties of the composite, attained through improved wetting and encapsulation of the fibers, as a result of treatment of the fiber surface-etching of the poly(glycolic acid) fibers by exposure to mildly acidic surfaces with a coupling agent. Fiber surface treatment involved first the surface-etching of the poly(glycolic acid) fibers by exposure to mildly acidic conditions. Then, the resulting carboxylic acid groups on the surface of the fibers were further reacted with the functionalized coupling agent (Figure 5). 3-Methacryloxypropyltrimethoxysilane, shown below, was selected as the coupling agent because of its commercial availability (Huls) and its compatibility with the unsaturated matrix and the poly(glycolic acid) fibers. When placed in the acid/water solution, the silane was hydrolyzed to give the corresponding silanol, which was then available for reaction with the carboxylic acid groups on the fiber surface. The fiber surface was thus functionalized with pendent methacryloyl groups which were available for copolymerization with the fumarate double bonds during the matrix curing reaction. This served to chemically bond the fiber to the matrix and develop a more fully enhanced interphase region.

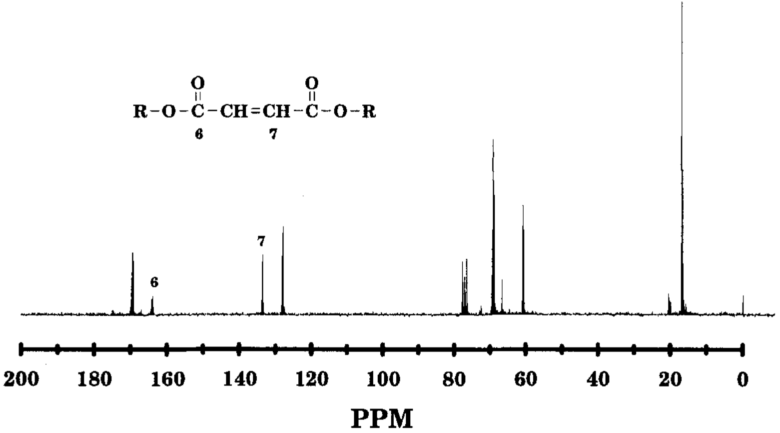

Figure 4: ^{13}C NMR spectrum for poly(D,L-lactide) fumarate

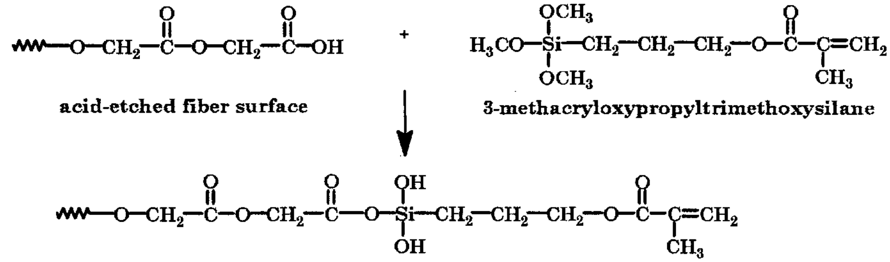

Figure 5: Reaction of acid-etched fiber surface with coupling agent

A statistically significant increase in the physical properties of the composite was deemed an indirect indication of improved wetting of the fiber surface with the matrix resin. It was observed that the composite fabricated with poly(glycolic acid) fibers which were acid-etched and pretreated with the coupling agent showed an average 41% increase in tensile strength; a representative sample, shown in Figure 6, displayed an increase from 73.9 MPa to 105.5 MPa upon fiber pretreatment. The composite fabricated with poly(glycolic acid) fibers which were acid-etched only possessed an intermediate tensile strength (87.2 MPa) which still showed a 18% increase over the untreated composite (Figure 6). Scanning electron microscopy (SEM) of the fracture surface also showed improved wetting of the fiber surface with the matrix resin. Figure 7 is a SEM of a tensile break surface of an untreated poly(glycolic acid) fiber-reinforced composite. The micrograph clearly shows fiber pull-out and a large gap at the fiber/matrix interface due to poor wetting of the fiber surface by the matrix. Poor wetting apparently reduced the overall strength of the composite by preventing efficient transfer of energy from the matrix to the load-bearing fibers. Figure 8 is a SEM of a tensile break surface for the treated poly(glycolic acid) fiber-reinforced composite. The absence of a gap at the interface region and the obvious decrease in the incidence of fiber pull-out implies that improved wetting of the fiber surface with the matrix was achieved. Additionally, the matrix resin appears to have better penetrated the fiber bundles since the individual fibers are more completely encapsulated.

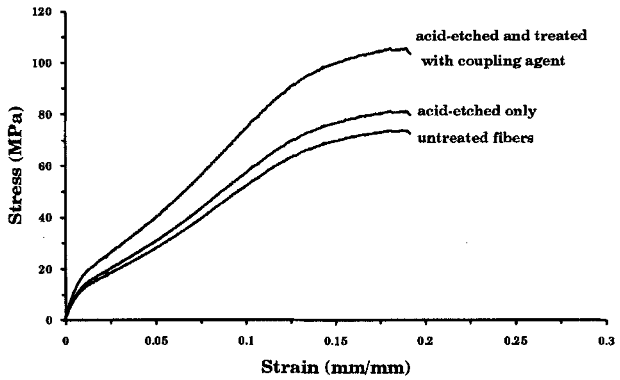

Figure 6: Stress-strain curves for bioabsorbable composites fabricated with poly(D,L-lactide) fumarate networks reinforced with treated and untreated poly(glycolic acid) surgical mesh.

Conclusion

Bioabsorbable composites were fabricated by reinforcing free radically cured poly(D,L-lactide) fumarate networks with poly(glycolic acid) surgical meshes. Through the selection of proper fiber pretreatments, including acid-etching and the incorporation of a coupling agent, better wetting of the fiber surface with the matrix resin was obtained, and thus the overall physical properties of the bioabsorbable composite were improved.

Acknowledgement: This research was supported in part by the National Science Foundation through Grant No. RII-8902064, the State of Mississippi, and the University of Southern Mississippi.

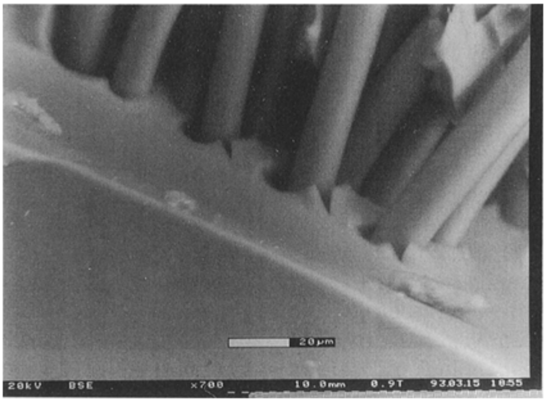

Figure 7: SEM of the fracture surface for the non-treated poly(glycolic acid) fiber reinforced bioabsorbable composite

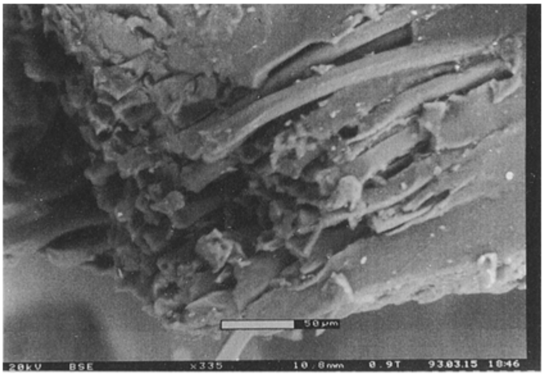

Figure 8: SEM of the fracture surface for the treated poly(glycolic acid) fiber reinforced bioabsorbable composite

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Accepted July 7, 1993 K