Two-phase controlled release of gentamicin from a bioabsorbable elastomeric film

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Statement of Purpose: Local delivery of antibiotics is an attractive strategy to prevent bacterial colonization of implant surfaces, and reduce the incidence of implant related infection in orthopedic surgery. This investigation evaluated the mechanical properties, drug release profile, and degradation profile of an elastomeric polymer film designed to allow delivery of an antibiotic directly at the surface of an orthopedic implant used in internal fixation.

Methods:

Film preparation: Films were produced from a bioabsorbable copolymer of glycolic acid (approximately 60%), caprolactone (20%), lactic acid (10%), and trimethylene carbonate (10%) (US Surgical, North Haven, CT). This copolymer was dissolved in DMSO at a concentration of 20% by weight, and either cast as a thin film onto a 20cm x 20cm glass plate, or mixed with 5% or 10% gentamicin sulfate and then cast. Cast films were dried in air at 60°C for a minimum of 12 hours to remove solvent, then removed from the glass plate and stored under vacuum for further testing. Finished films had a thickness of 0.06 ±0.01mm.

Test sample preparation: Samples for tensile testing, *in-vitro* degradation, and drug elution testing were cut from cast films. Tensile samples were 10mm wide by 80mm long per ASTM D882-02. For the remaining testing, discs 19 mm in diameter were used.

In-vitro degradation: Samples were weighed and placed into vials containing phosphate buffered saline solution (PBS) at 37°C for 1d, 4d, 7d and weekly up to 1 month. Fresh PBS was changed weekly and the pH was monitored. At test times, the samples were removed from the solution, freeze dried, and weighed again. The average molecular weight of each sample was also measured by gel permeation chromatography equipped with refractive index detector and viscometer. The mobile phase was DMSO, at 1.0 mL/min flow rate with polyethylene oxide narrow standards.

Tensile testing: Tensile samples were tested in tension to failure on an Instron test stand (model 3342) at 20mm/sec, dry and at room temperature, per ASTM D882-02.

Drug release testing: Drug release testing was performed in PBS at 37°C. Concentration of gentamicin in solution was measured at 15 min, 30min, 1hr, 2hr, 4hr, 6hr, 1d, 2d, 4d, 7d and weekly up to one month, using fluorescence polarization immunoassay technique (TDxFLx, Abbott Laboratories).

Results/Discussion:

Tensile properties: Initial tensile properties of the films tested at t=0 are shown in table 1.

Table 1: Initial tensile properties of films

	Modulus (MPa)	tensile strength (MPa)	Elongation at break
control	390.2 ± 29.2	31.4 ± 6.6	365%
5% GS	294.6 ± 31.5	20.6 ± 2.3	288%
10% GS	256.4 ± 33.8	16.4 ± 1.7	230%

Drug release:

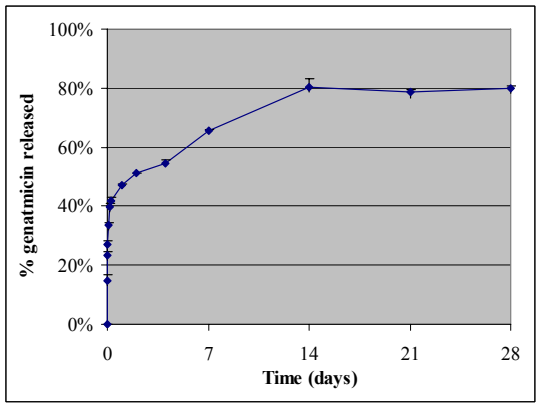

Figure 1: Elution profile of gentamicin in PBS at 37°C

In-vitro degradation:

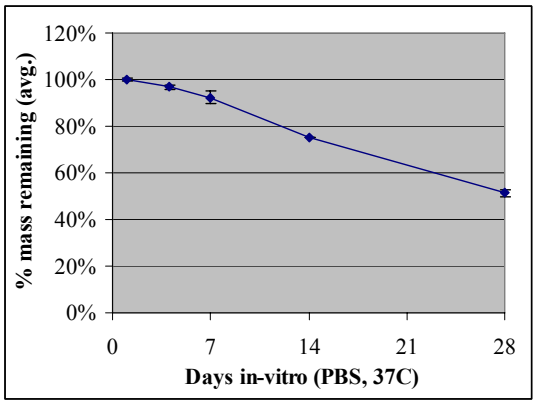

Figure 2: Mass loss *in-vitro* in PBS at 37°C

Elution of gentamicin from this elastomeric bioabsorbable copolymer exhibits a combination of initial burst release, followed by a sustained elution over the initial 2 weeks of implantation time. Incorporation of gentamicin causes a 34% and 48% reduction in initial tensile strength, and a 24% and 34% reduction in initial tensile modulus for the 5% and 10% loading respectively. For all formulations, the elongation at break is over 200%

Conclusions: This copolymer is an appropriate candidate for a bioabsorbable drug-delivery film requiring elastic properties and a sustained drug release profile.