Fabrication of biodegradable polyurethane/poly(lactide-co-glycolide) nanofibrous sheets with controlled antibiotic release via two stream electrospinning

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Introduction

Trauma to the extremities can lead to edema and compartment syndrome, which can trigger tissue necrosis and permanent loss of function. Fasciotomy is the preferred treatment method for compartment syndrome in the field, but at the expense of an open injury. To reduce the contamination and infection risk associated with fasciotomy, we have developed a biodegradable elastomeric patch capable of controlled antibiotic release. Specifically, we combined poly(ester urethane) urea (PEUU) nanofibers with poly(lactide-co-glycolide) (PLGA) nanofibers loaded with the antibiotic tetracycline hydrochloride (tet), by concurrently electrospinning two polymer streams to obtain a fibrous elastic sheet. The mechanical properties, morphology, tet release profile and antimicrobial activity of this composite material were investigated.

Materials and Methods

PEUU was synthesized from polycaprolactone diol and 1,4-diisocyanatobutane with chain extension by putrescine as previously reported [1]. PLGA (50/50, Mw=40,000-75,000) and tet were purchased (Sigma). PLGA (15wt%) in hexafluoroisopropanol (HFIP) was blended with tet (1, 5, 10 and 20wt% to PLGA). PEUU (6wt%) in HFIP was electrospun over a 20cm distance at 1.5 mL/h [2]. Meanwhile, PLGA-tet was concurrently electrospun from 13cm at 0.5mL/h. A stainless steel rod (1.9cm diameter) rotating at 250 rpm and translating 8-cm along its axis at 8 cm/s was the collecting surface.

Scanning electron microscopy (SEM) was utilized to characterize the fibrous morphology. Tensile testing was completed according to ASTM D638-98. PEUU fiber content was quantified by weighing after dissolving PLGA-tet fibers with acetone. Sheet patches were immersed in 5ml phosphate buffered saline (PBS) at 37°C to quantify tet release. At each time point, 5ml release solution was removed and 5ml fresh PBS was added. The tet concentration was measured by UV absorbance at 360nm. Patches (6mm diam) were directly placed on agar plates seeded with *E. coli* or *S. aureus* to quantify antimicrobial activity by measuring inhibition diameters. PEUU sheets without PLGA or tet were used as a control.

Results

Electrospun PEUU/PLGA-tet sheets at all tet concentrations studied possessed continuous fiber morphologies, typified by PEUU/PLGA-tet 20% (**Fig. 1**). The PEUU/PLGA-tet sheets did not show a weakening effect with added tet wt% and had tensile strengths of 3.9-5.2 MPa and strains at failure of 45-60%. After 1.5h burst release of tet into PBS at 37°C, the released tet concentrations decreased with time, but remained in the 0.1-0.5μg tet per ml PBS per mg polymer at time points up to 168 h (**Fig. 2**). A tet loading dose effect on the tet release concentrations was apparent. Inhibition diameters on agar plates of *E.coli* and *S. aureus* from polymer patches ranged from 16-29mm and increased with tet content (**Fig. 1**).

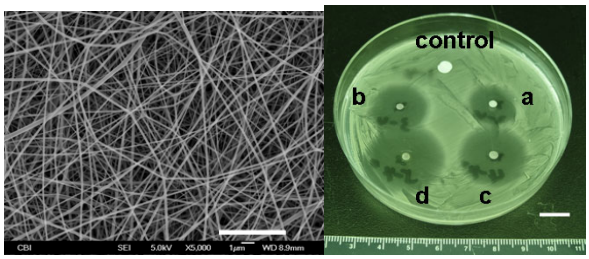

Fig. 1 SEM image of PEUU/PLGA-tet20% (left, bar=5μm) and macroscopic image of *S. aureus* inhibition diameters of PEUU/PLGA-tet 1%(a), 5%(b), 10%(c) and 20%(d) at 24 h (right, bar=10mm).

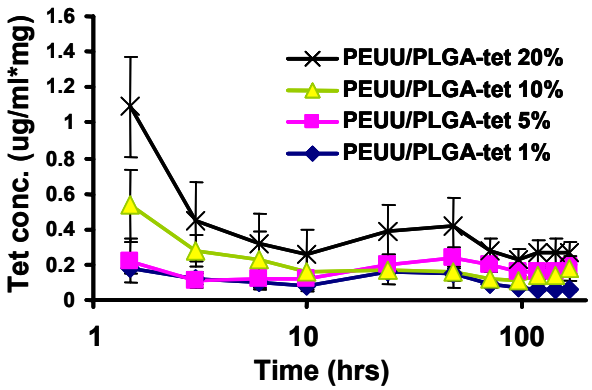

Fig. 2 Tet release from variably loaded PEUU/PLGA-tet sheets in PBS at 37°C after a 1.5 h burst release.

Conclusions

PEUU and tet-loaded PLGA nanofibers were concurrently deposited with two stream electrospinning to create a biodegradable, elastomeric antibacterial patch that could be applicable in fasciotomy management. The combination of the two fiber types allowed the slower controlled release properties of the PLGA fibers to be blended with the flexible mechanical properties of the PEUU fibers to form a composite with improved functionality.

Acknowledgements & References

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[1] Guan JJ et al. *J Biomed Mater Res* 61:493 (2002).
[2] Stankus JJ et al. *J Biomed Mater Res* 70:603 (2004).