Electrospun biodegradable, elastomeric poly(ester urethane) urea fibrous scaffolds with paclitaxel release for vascular bypass applications

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Introduction

The controlled release of anti-proliferative agents is widely used to limit intimal hyperplasia in the setting of coronary stents. A smooth muscle cell hyperplastic response is also problematic in vein grafting in the extremities and coronary locations. We have recently reported the use of a biodegradable elastic electrospun wrap to mechanically protect vein grafts from sudden arterial pressure-driven expansion [1]. Here we examine the potential to load such an electrospun wrap with the antiproliferative agent paclitaxel (taxol). The impact of paclitaxel loading on wrap mechanical properties and morphology, as well as the temporal release and bioactivity of paclitaxel were measured.

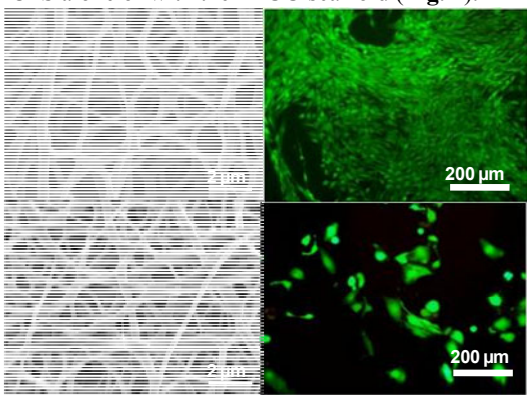
Materials & Methods

PEUU was synthesized from polycaprolactone diol and 1,4-diisocyanatobutane with chain extension by putrescine as previously reported [2]. PEUU in hexafluoroisopropanol (HFIP) was blended with taxol (0, 2.5, 5 and 10 wt% to PEUU). The mixed solution (6%) was electrospun over a 15 cm distance at 1 mL/h [3]. A stainless steel rod (1.9 cm diameter) rotating at 250 rpm and translating 8-cm along its axis at 8 cm/s was the collecting surface.

Scanning electron microscopy (SEM) characterized scaffold morphology. Taxol physical status in the polymer was determined with DSC at a heating rate of 20°C/min. Tensile testing was completed according to ASTM D638-98. Scaffolds were immersed in 10 mL 10(v/v)% ethanol/phosphate buffered saline (PBS) at 37°C to quantify taxol release. At each time point, 10 mL solution was removed, taxol conc. measured by UV absorbance at 230 nm, and 10 mL fresh ethanol/PBS added. Scaffolds with variable taxol loading (5 mm diam) were directly placed in 24-well culture plates pre-seeded with rat smooth muscle cells to quantify proliferation inhibition by mitochondrial assay. Culture medium was changed every 2 days. PEUU electrospun without taxol and tissue culture polystyrene (TCPS) were used as controls. Cell morphology was observed after live/dead staining.

Results & Discussion

Electrospun PEUU/taxol sheets at all taxol concentrations studied possessed continuous fiber morphologies (**Fig. 1**). DSC data indicated loaded taxol was in a molecular dispersion or solid solution state. PEUU and PEUU/taxol scaffolds at 2.5 and 5% taxol loading had tensile strengths of 6-7 MPa and breaking strains of 299-359%. At 10% taxol loading a slightly lower tensile strength (5 MPa) and a higher strain-to-failure (407%) were found compared to unloaded material ($p<0.05$), and this is likely attributed to altered intermolecular interactions. Loaded scaffolds showed continuous taxol release after a 10-30% burst at day 1 (**Fig. 2**). All taxol-loaded PEUU scaffolds markedly inhibited SMC proliferation during the 1 wk culture period. By day 5, SMC morphology was rounded and polygonal in the presence of PEUU/taxol, while near confluent SMC layers were formed on TCPS alone or with the PEUU scaffold (**Fig. 1**).



Fig, 1 (Left) Scaffold morphology for PEUU (top) and PEUU/taxol5% (bottom). (Right) SMCs at 5 d culture under PEUU (top) or PEUU/taxol5% (bottom).

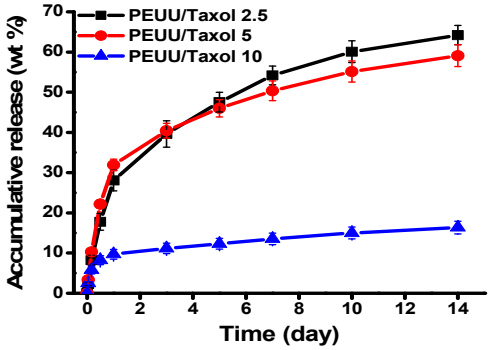


Fig. 2 Taxol release from variably loaded PEUU/taxol sheets in 10% ethanol/PBS at 37°C**.**

Conclusions

PEUU and taxol were successfully combined by electrospinning to create a biodegradable, elastomeric fibrous scaffold that exhibited bioactivity against SMC proliferation. This electrospun material, when wrapped around a venous segment prior to arterial bypass placement might be able to resist or delay the onset of intimal hyperplasia leading to graft failure.

Acknowledgements & References

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