Nitric Oxide-Releasing Nanoparticle/Polymer Microfiber Composites

Jessica A. Nash, Peter N. Coneski, Daniel A. Riccio, and Mark H. Schoenfisch
Department of Chemistry, University of North Carolina, Chapel Hill, North Carolina

Statement of Purpose: The proven antimicrobial and wound healing properties of nitric oxide (NO) make NO release a particularly interesting approach for the design of biocompatible materials.[1] Although numerous NO-releasing material formulations have been prepared, the lack of material diversity limits potential applications. Electrospinning is a versatile technique for the preparation of micro and nano scale materials.[2] The high porosity and surface area inherent to electrospun fibers make them ideal candidates for applications such as drug delivery, tissue engineering scaffolds, wound dressing materials, and medical device coatings.[3] Microfibers with NO-release capabilities would thus be expected to improve biocompatibility and tissue integration. Herein, we examine the incorporation of NO releasing materials into electrospun microfibers. The effects of fiber size, morphology, and polymer composition on NO release characteristics are reported.

Methods: Polymers were dissolved in a 3:1 mixture of tetrahydrofuran (THF)/ N,N'–dimethylformamide (DMF). Nitric oxide donors were suspended or dissolved in methanol (MeOH) by sonication and then transferred to polymer solution (final mixture 3:1:1 THF/DMF/MeOH). To ensure a homogenous mixture, solutions were vortexed briefly. The polymer solutions were placed in a syringe with a 22 gauge blunt tip needle atop a syringe pump. Electrospinning was performed at a flow rate of 15 µL/min and an applied voltage of 15 kV. Fibers were collected on a grounded, conductive plate covered with aluminum foil that was positioned 15 cm from the tip of the needle. Surface morphology and diameters of fibers were evaluated using Electron Microscopy (EM) (figure 2). Nitric oxide-release kinetics were examined using a chemiluminescence NO Analyzer (NOA).

Results: Tecoflex polyurethane, Tecophilic polyurethane and poly(vinyl) chloride (PVC) were used for the fabrication of microfibers. To examine the influence of polymer type and fiber size on NO release kinetics, S-nitrosothiol-modified nanoparticles (RSNO-SNP) were incorporated into fibers. Release of NO was measured for at least one week. As expected, the incorporation of nanoparticles into fibers was found to extend NO release (>7 d) when compared to nanoparticles alone (~ 2 d).

Generally, fibers electrospun from 12% solutions required a longer time to maximum flux of NO ($[NO]_{max}$) compared to fibers prepared from 8% solutions. Increased diffusion times through the material may be attributed to the increasing diameter for fibers prepared from higher concentrations of polymer solution. Because S-nitrosothiols decompose thermally, release of NO is expected to be mediated mainly by fiber diameter. Measurement of fibers prepared from 12 wt% solutions of PVC and Tecophilic PU showed that diameters did not vary significantly for the two polymer systems (537 ± 211 nm and 517 ± 158 nm respectively). There was no significant difference in NO flux for fibers prepared from different polymers after a few hours (Fig 1). For N-diazeniumdiolate NO donors, which decompose by a proton initiated mechanism, it has been shown that varying hydrophilicity of polymer solution significantly affects rate and duration of NO release.[4]

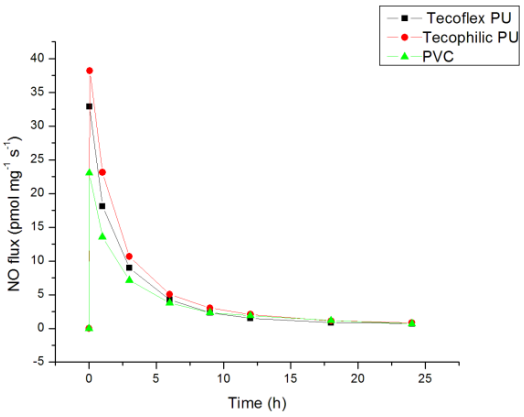

Figure 1(above): NO flux for fibers prepared from 12% polymer solutions. Nanoparticles added were 20% of polymer weight, 16.7% weight of final nanoparticle/polymer composite.

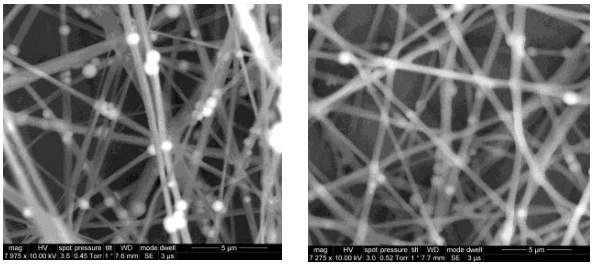

Figure 2: ESEM images of electrospun fibers doped with RSNO-SNP. Fibers spun from 12 wt% PVC solutions. (left), and 12 wt% Tecophilic solutions (right).

Conclusions: Combining the advantages inherent to electrospun materials with NO release capabilities has the potential to generate unique nanofibrous scaffolds with diverse medical applications. The incorporation of NO donors into electrospun polymer microfibers has been shown to allow for controlled release of nitric oxide. Fiber morphology and diameter may play a role in the rate and duration of NO release, with increased fiber diameter delaying $[NO]_{max}$. Future work aims to investigate other polymer/NO donor systems as a means to fabricate materials with diverse compositional and NO release characteristics.

References: (1) Hetrick, E. M. et al., *Chemical Society Reviews* **2006**, *35*, 780-789. (2) Teo, W. E. et al., *Nanotechnology* **2006**, *17*, R89-R106. (3) Agarwal, S. et al., *Polymer* **2008**, *49*, 5603-5621 (4) Coneski, P. N., et al., **2010**, submitted

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