Nitric Oxide-Releasing Electrospun Polyurethane Wound Dressings

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Statement of Purpose: As the prevalence of diabetes grows worldwide, the associated healthcare costs place an increasingly substantial financial burden on society. Of the medical complications associated with diabetes, the propensity for developing chronic wounds poses a serious health risk to the patient. Successful treatment of chronic wounds is hindered by infection. The design of wound dressings capable of administering antibiotics and/or antimicrobial agents thus continues to be a major research focus. To date, most methodologies have proven inadequate at preventing infection and some (e.g., silver) have been shown to foster bacterial resistance, necessitating the development of alternative therapeutics. Herein, we describe the fabrication of antibacterial wound dressings that incorporate nitric oxide (NO) donors within electrospun polyurethane fibers.

Methods: All chemicals were analytical-reagent grade and used as received. Pure NO gas was purchased from Praxair (Sanford, NC). Tecoplast, tecoflex, hydrothane, and tecophilic polyurethanes were purchased from Thermedics (Woburn, MA). Generation 4 poly(amidoamine) dendrimers were modified with octyl, dodecyl, and octylQA moieties via a ring-opening reaction at the dendrimer peripheral primary amines. The resulting secondary amines were modified with N-diazeniumdiolate NO donors to yield NO-releasing dendrimers with varying hydrophobicity and NO-release kinetics. NO release was measured in real time using a chemiluminescent NO analyzer (Boulder, CO) at pH 7.4. Electrospinning solutions were prepared by dissolving polyurethane in a THF/DMF solutions with the NO-releasing dendrimers added in methanol. The resulting polyurethane/dendrimer solutions were electrospun to yield NO-releasing fibrous mats as antibacterial wound dressings. Nitric oxide-release properties were tuned by altering the dendrimer modification, NO donor weight percent, and/or the polyurethane identity.

Results: Before incorporation into electrospun fibrous mats, control and NO-releasing dendrimers were fully characterized. The modification of the dendrimer scaffold was confirmed using ^{1}H NMR spectroscopy, with approximately 70% of the terminal primary amines being modified with hydrophobic functionalities (Figure 1).

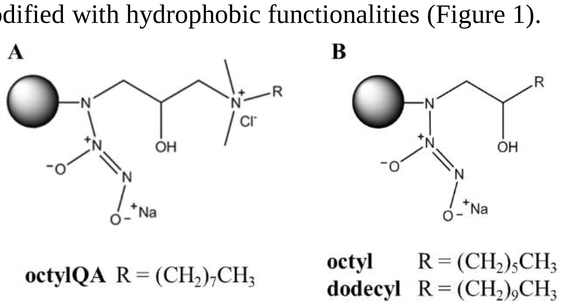

Figure 1. Structures of A) QA-modified and B) alkyl chain-modified G4 PAMAM dendrimers.

Addition of the QA moiety was confirmed using XPS spectroscopy. The hydrophobic dendrimer scaffolds were then modified with N-diazeniumdiolate NO donors to yield dendrimers with varied NO-release kinetics but similar NO payloads (Table 1).

Table 1. NO-release characteristics at pH 7.4

	t[NO] (µmol/mg)	$t_{1/2}$ (min)	t_d (h)
G4 octyl/NO	0.89 ± 0.04	23 ± 7	10 ± 1
G4 dodecyl/NO	0.90 ± 0.12	33 ± 2	11 ± 1
G4 octylQA/NO	1.01 ± 0.05	113 ± 4	16 ± 1

The physical and chemical properties of polyurethane, dendrimer-doped, and NO-releasing fibrous mats were characterized to assess the feasibility of using electrospun polyurethanes as wound dressings. Physical characterization and NO-release properties were evaluated as function of polyurethane, alkyl chain length (i.e., G4 octyl vs G4 dodecyl), NO-release half-life (i.e., G4 octyl vs G4 octylQA), and amount of incorporated dendrimer. Control and NO-releasing dendrimers were evenly distributed throughout the electrospun fibers with minimal leaching. Further, the incorporation of dendrimers into the polyurethane fibers had little effect on the physical properties of the fibrous mats. For example, increasing the concentration of G4 octyl dendrimers doped into Tecoflex did not alter the water absorption capabilities of the resulting fibrous mats (Figure 2).

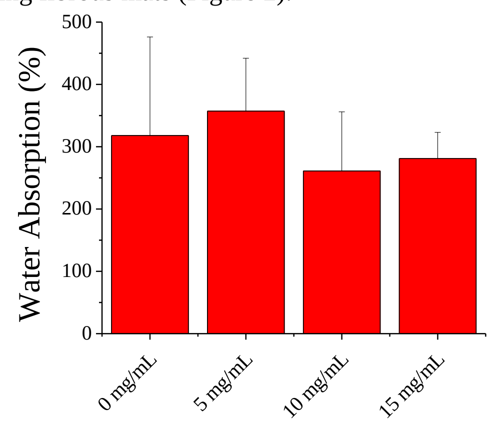

Figure 2. Water absorption (by weight) of Tecoflex polyurethane fibers with G4 octyl dendrimer dopant.

Conclusions: These studies demonstrate the potential of NO-releasing electrospun polyurethane fibers as antibacterial wound dressings. Both control and NO-releasing dendrimer-doped fibrous mats exhibit properties essential for wound dressings, including high water uptake, porosity for gas permeation, and minimal dopant leaching. Future work will evaluate the antibacterial action of the NO-releasing wound dressings against bacteria commonly associated with chronic wounds.