Surfactant Interactions and Solvent Solubility Modulate Small Molecule Release from Emulsion Electrospun Fibers

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Statement of Purpose: Electrospinning is a technique widely used to develop scaffolds that mimic the native environment of the extracellular matrix (ECM) and can be tuned for the controlled release of small molecule drugs. Emulsion electrospinning offers increased stability, encapsulation efficiency, and bioavailability, as well as controlled release of drugs compared to traditionally electrospun solutions. Controlling drug release kinetics from fibers is imperative to release at therapeutically effective levels while minimizing adverse, unwanted side effects. Rate and method of drug release from electrospun mesh depends on the fiber volume fraction, fiber diameter, fiber porosity, as well as the compatibility of the drug with fiber material and surrounding solvent. Drug release occurs via two different mechanisms: 1) a burst release, associated with unpredictable and uncontrolled kinetics and 2) a controlled release associated with a predictable, sustained release that could be tailored to personalized conditions. Previously, no studies examined drug release from electrospun fibers while controlling for fiber diameter and volume fraction. This study examined the role of drug hydrophobicity in electrospun fibers with no surfactant, surfactant, and water-in-oil (w/o) emulsions independent of fiber diameter and volume fraction.[1]

Methods: Polymer solutions were formulated from 20 w/v % PCL dissolved in 3:1 $CHCl_3$:DMF. Span 80 at 30 w/w% was added to both polymer solutions containing no internal phase and emulsions containing 8 w/o % internal phase. Either Nile Red (NR) or Rhodamine B (RB) was added to solutions and emulsions at a concentration of 1 mg/mL whereby solutions containing no surfactant, surfactant, and emulsion with NR are denoted as NN, NS, NE and those containing RB are denoted as RN, RS, RE, respectively. These solutions were electrospun using a Harvard Pump Apparatus with a volumetric flow rate of 1.5 mL/h, a distance from needle tip to collection plate of 20 cm, and an applied voltage of 18kV. Fiber diameter and volume fraction were determined using SEM imaging and analyzed using Diameter J. Each electrospun scaffold was sampled in triplicate using an 8mm histology punch. Each punched-out specimen was weighed to normalize for differences in mesh thickness. Drug encapsulation was determined by completely dissolving 8mm specimens in $CHCl_3$ which were then analyzed using a Biotek Cytation 5 plate reader to determine fluorescence. Specimens containing NR or RB were placed in 1 mL of either Ethanol or RO water, respectively. At 0.5, 1, 1.5, 2, 2.5, 2, 4, 5, 10, 15, 30, 45, and 60 minutes, solvent was removed and stored temporarily, and original solvent levels restored in specimen's tube. Each sampled time point of NR and RB was pipetted onto a 96 well plate in triplicate and fluorescence was analyzed using a plate at excitation wavelengths of 554 ± 20 nm and 553 ± 20 nm and emission wavelengths of 638 ± 20 nm and 627 ± 20 nm, respectively. Encapsulation and release concentrations were determined using standard curves of both fluorescent small molecules.

Results: The fiber diameter and volume fraction were notably not statistically significant across all groups which is essential to accurately compare drug release rates between each group. Fibers were predominantly cylindrical and uniform with a smooth surface topography (Figure 1A and 1D). In samples containing NR, loading was statistically significant across all groups (Fig 1B) with encapsulation amounts decreasing from NN, to NS, and NE. All groups of NR exhibited similar burst release effects indicating that the molecule was primarily located on the surface of the fiber likely due to either electrostatic repulsion or phase separation during the electrospinning process (Fig 1C). In RB, there was no difference seen in drug loading between RN and RS groups, however significantly increased drug encapsulation was observed in RE (Fig 1E). In groups of RB, significantly less burst release was observed in RS and RE compared to the RN control (Fig 1F). This is due the increased solubility of RB upon introduction of both surfactant and aqueous internal phase.

***Conclusions and Future Work*:** Overall, these results illustrate the role of molecular interactions between varying degrees of drug hydrophobicity with both surfactant and emulsion internal phase as well as show that drug release rates from emulsion electrospun fibers can be controlled by varying those parameters. In future work, we will extend the time period of release analysis as well as investigate the relationship between internal phase volume fraction and hydrophilic drug loading.

References:

1. P Johnson et al. *AIChE J. 2021; e17470.*

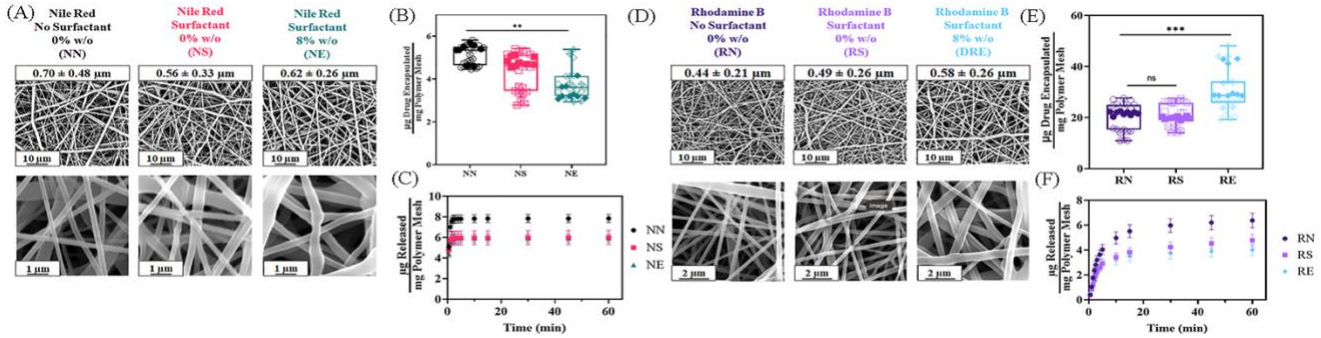

Figure 1. (A, D) SEM images and fiber diameters for NN, NS, NE, RN, RS, and RE specimens. (B, E) Encapsulation efficiency of NR and RB in NN, NS, NE, RN, RS, and RE groups. (C, F) Mass of drug release normalized with specimen mass over time.