Tailored Drug Release from Nanofibre-based Wound Dressings

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Introduction:

Despite the native healing capability of the skin, many patients suffer from various complications, caused by incomplete or faulty healing, often requiring therapeutic interventions. Treatments including autografts and advanced scaffolds have been well-documented. Recently, incorporating bioactive components such as drugs in scaffolds have become popular for aiding regeneration processes. Among the various forms of skin scaffolds, nanofibrous structures have attracted attention due to its large surface area and structural resemblance to native extracellular matrix. Significant process has been made after the pioneering work on drug-loaded nanofibres in the early 2000's, as many groups have since demonstrated different rates of antimicrobials and growth factors release from nanofibrous dressings[1]. Building on the success in wound dressing development, our goal is to design nanofibre-based dressings that can be tailored to address different stages of healing. Rather than loading drugs into different materials and observing release, a need-based design approach is required to achieve highly customizable release properties. As the first step in defining needs for the dressing design, we aim to develop a nanofibre system that incorporates hydrophilic drugs, which are often associated with burst release due to water solubility, and facilitate stable release over a range of 1- 3 days, a suitable range for addressing the early to intermediate stage of the wound healing process. This can be accomplished by modifying degradation and diffusion properties of polymer matrices. Success in tailoring drug release behavior from nanofibres can not only lead to methods for designing dressings that suits different needs, but also open opportunities for use in other tissues.

Materials and Methods:

The drug used in this study is a hydrophilic model compound provided by the BC Professional Firefighter Burn and Wound Healing Laboratory. The model drug was prepared in an aqueous solution, and polyvinyl alcohol (PVA) was selected as the carrier for its water solubility. The drug and polymer mixture was fabricated into nanofibers by electrospinning at a voltage of 17 – 20kV. As PVA is highly water soluble, the first step in controlling drug release is to modify the degradation rate of the matrix. The electrospun drug-loaded PVA was heat treated at 100 - 120°C for two hours. In addition, fluid penetration into the scaffold was delayed by adding an envelope of the less degradable polycaprolactone (PCL). Tortuosity was further controlled by changing the porosity of the PCL shell layer, from varying nanofibre sizes to converting the layer into a solid film through dip-coating. To confirm nanofibrous morphology and its maintenance after heat treatment, scanning electron microscope (SEM) images were taken. Drug release was measured by first incubating nanofibres in a phosphate buffered saline (PBS) solution for predetermined durations, and then extracting an aliquot of the PBS which was then analyzed for drug contents spectrometrically by light absorbance.

Results:

Figure 1 compares the release behaviors of modified drug-loaded scaffolds. Immediate burst release was observed from the as-electrospun PVA (SEM image in Figure 2) as expected. The burst

release was significantly reduced through heat treatment, although some of the drugs also became entrapped due to formation of insoluble crosslinked PVA networks. Envelopment with nanofibrous PCL (SEM in Figure 3) was also shown to have significant impact on reducing burst release, and the effect was more pronounced as the PCL nanofibre shell was replaced with a film.

Release results were also fitted to common release models to determine release mechanisms. It was observed that heat treatment and PCL envelopment both caused the drug release behavior to change from zero order to a two-phase behavior, with the first phase resembling Higuchi's model and the second resembling the Korsmeyer-Peppas model with a diffusion coefficient of 0.5-0.6. It was also noticed that when the PCL nanofibre shell around the drug-loaded PVA was replaced with a solid film, the release returned to a one-phase behavior, but resembling the Korsmeyer-Peppas model with a diffusion coefficient of 0.4.

Discussion:

The transition from zero-order to the Higuchi and Korsmeyer-Peppas release behaviors upon heat treatment or PCL envelopment indicates a change from release driven by polymer erosion to one that involves a combination of erosion and drug diffusion from the polymer matrix [2], as a result of delaying the dissolution of PVA in water. Upon replacing the nanofibrous PCL shell with a PCL film, dissolution of PVA was further inhibited, leading to a release driven predominantly by diffusion, as indicated by a lower Korsmeyer-Peppas diffusion coefficient. Furthermore, to prevent compromise in nanofibrous surface properties a PVA layer coated with PCL film can easily be integrated into a nanofibrous backing that can provide the handleability required. The current study is a first step in facilitating customizable hydrophilic drug release that may be useful in tissue regeneration. While the choice of polymer matrix was limited by drug compatibility, results showed that modifying the balance between erosion and diffusion driven release is effective in obtaining tailorable lengths ranging from 1 – 3 days.

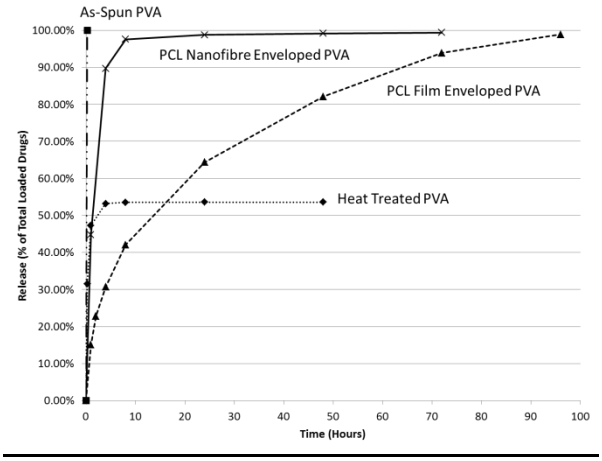

Figure 1: Comparison of release from PVA with different modifications

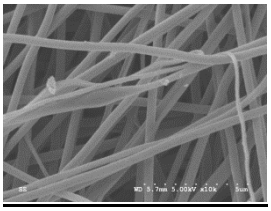

Figure 2: SEM Image of drug-loaded PVA nanofibres

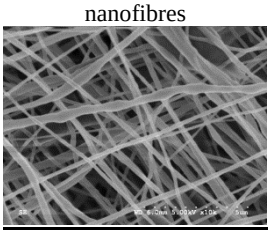

Figure 3: SEM Image of nanofibrous PCL shell

References:

1. Hromadka, M., et al., *Nanofiber Applications for Burn Care.* Journal of Burn Care & Research, 2008. 29(5): p. 695-703.
2. Siepmann, J. and N.A. Peppas, *Higuchi equation: Derivation, applications, use and misuse.* International Journal of Pharmaceutics, 2011. 418: p. 6-12.