Microfibrous Non-Woven Scaffolding for Liquid Drug Delivery

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Statement of Purpose: Continuing pursuits at Poly-Med regarding development of controlled drug delivery systems and growing interest in electrospun materials has led to our pursuit of a microfibrous non-woven scaffolding produced through electrospinning techniques for drug delivery. Through our research, we present a scaffold having excellent drug handling characteristics and physical properties conducive to manufacturing drug delivery devices. Current data gathered from testing has led to the production of multiple lots in order to ensure reproducibility of both electrospinning technique and drug delivery of final product.

Methods: To create the scaffold, a mixture was first prepared with solids consisting of a PEG 35,000/L-Lactide based polymer, PEG 4600, and a Glycolide/TMC/Caprolactone/L-Lactide based polymer all dissolved in methyl acetate. This mixture was then electrospun onto a stainless steel cylinder using a needle-based electrospinning process to create a 1.0-1.2 mm thick, 500 cm^2 sheet. The electrically grounded cylinder was slowly rotating and placed 10-15 cm away from the needles. The solution was held in two syringes with 18 G blunt-end needles attached. A voltage of 21.0 kV and current of 0.009 mA was applied to the needles. The resulting sheet was then pressed using a novel heated limited pressing method to produce a uniform 0.8 mm thickness. This is important due to the inherent relative non-uniformity of the electrospun material's thickness and the concurrent need for appropriately sized material for drug delivery.

After pressing, the density of the scaffold was calculated. The drug solution absorption of the scaffold was tested by measuring the time needed for a 1 cm^2 sample of the scaffold to completely absorb 100 µl of a 0.5M hydrophilic drug solution into the electrospun matrix.

In addition, the drug delivery of the scaffold was tested in triplicate using 1 cm^2 samples of the scaffold each loaded with 50 µl of a 0.5 M hydrophilic drug solution. These samples were then immersed in a 7.2 pH potassium phosphate buffer bath with 200 µl of the buffer solution being drawn at 10 time points from 0 to 30 minutes. The samples removed were diluted with 800 µl of saline, and then tested using HPLC. The relationship between amount of drug released and time was plotted.

The scaffold was further tested by hand manipulation under wet and dry conditions to qualitatively determine the abrasion properties. These mechanical properties are important for the material to maintain drug delivery system integrity.

Results:

Using standard test methods, the *in-vitro* release profiles for the scaffold at various time points are outlined in Figure 1. The release properties shows a near linear profile for the first 80% of drug released at up to 10 minutes and complete delivery by 30 minutes. The drug absorption properties of each lot were tested as described. The results of these tests are depicted in Figure 2. This figure demonstrates the exceptional drug absorption that decreases with decreasing density.

Based on the qualitative mechanical testing performed, the electrospun scaffold was determined to be non-friable under both wet and dry states.

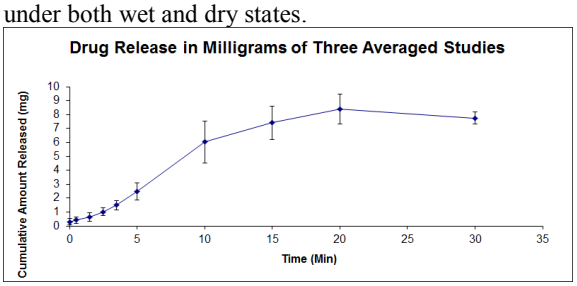

Figure 1. Drug release from electrospun scaffold

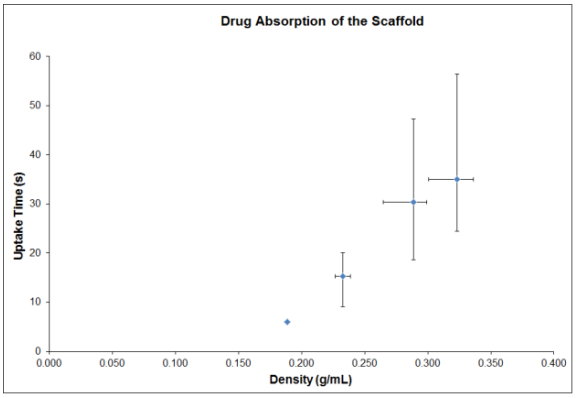

Figure 2. Drug solution absorption time in seconds with varying scaffold density

Conclusions: Poly-Med has developed an electrospun material that has number of flexible attributes in terms of ease of preparation/scale-up, as well as drug loading, handling, and delivery. We believe this system is an ideal and versatile platform for drug delivery. With the novel material sizing and production techniques playing a large part in its success, we are currently expanding the number of absorbable polymers that may be developed. As more lots of the electrospun material are produced, the properties of the material will be further tested to develop a better understanding of this novel scaffold.

Positive client reviews have demonstrated that the electrospun product is of high quality, and there is a large desire for an increase in production.

References:

1. Shalaby, S.W. et al., US patent 7,070,858 (2006)
2. Shalaby, S.W. et al., US patent 6,794,485, (2004)
3. Shalaby, S.W., US patent 6,462,169, (2002)
4. M. S. Taylor, *Study of Electrospinning of Property Modulated Biomedical Microfibers*. Thesis. Clemson University, 2008.
5. Shalaby, S.W. et al., US patent appl. 11/599,695 (2007)