Effect of Hydrophobicity on Release of Hydrophilic Therapeutics from Hydrogel-Electrospun Fiber Mat Composites

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Statement of Purpose: Poly(ethylene glycol) PEG-based hydrogels have been widely applied as controlled delivery vehicles. In particular, degradability of PEG-based hydrogels can be modified with the introduction of degradable segments, such as hydroxyacids (e.g., poly(lactic acid) PLA) [1]. The relationship between the chemical and physical properties of hydrogels and their swelling and release behaviors has been explored for decades. However, non-linear release profiles with high initial release (burst effect) are common, especially for hydrophilic therapeutics with small molecular weights (MWs) [2]. Burst release is usually undesirable because of potential local cytotoxicity, inefficient delivery of expensive drugs, short release duration, and loss of therapeutic bioactivity.

One promising strategy to reduce burst release is to introduce hydrophobic electrospun fiber mats (EFMs) (e.g., poly(ε-caprolactone) PCL) as buffering layers. This design provides a more linear and longer release profile with significantly reduced burst effect. However, the mechanism behind these improvements is unclear. One possibility is that the presence of external hydrophobic EFMs hinders release of hydrophilic drugs through hydrophobic-hydrophilic interactions. Alternatively, the diffusional path length is also increased, and could lead to the change in release profiles. Thus, to evaluate these hypotheses, we examined swelling and release behaviors of hydrogel-EFM composites composed of EFMs with different thicknesses and hydrophobicity.

Methods: PCL EFMs with thicknesses of 300 μm, 800 μm and 1100 μm were fabricated by altering EFM deposition time. PCL/PEGPCL core/shell, fluorinated PCL, and acrylic acid-treated PCL (PCL-AAc) EFMs with a thickness of 1100 μm were prepared through core/shell co-electrospinning, plasma surface treatment, and AAc graft polymerization, respectively. EFM hydrophobicity, average fiber width, mean pore size, and porosity were characterized using contact angle goniometry, scanning electron microscopy (SEM), and the ethanol displacement method. PEGPLA hydrogel-EFM sandwich composites (EFM+Gel+EFM) were constructed by UV photo-polymerization. Then, composite thickness, total area, and swollen and dry volumes were compared. Release kinetics of bovine serum albumin was studied over 8 weeks to estimate the influence of EFM hydrophobicity and thickness on hydrophilic therapeutic release behavior.

Results: EFM characterization confirmed no significant difference in average fiber width, mean pore size, or porosity for all six EFMs studied. Hydrophobicity of PCL EFMs increased slightly as EFM thickness increased. Fluorinated PCL EFMs exhibited the greatest hydrophobicity, whereas PCL/PEGPCL core/shell and AAc-treated PCL EFMs were super-hydrophilic, with water contact angles close to 0º. Swelling behavior studies demonstrated that although the total area ratio and volumetric swelling ratio of composite materials were smaller than those of PEGPLA hydrogels, indicating the effective constraint of external EFMs on hydrogel swelling in radical direction (r); the thickness ratio of composite materials, especially for those with hydrophobic EFMs, was higher than that of PEGPLA hydrogels, implying reduced interpenetration of the hydrophilic hydrogel into the hydrophobic EFM network. Correspondingly, longer release profiles with smaller burst effect could be achieved by increasing the thickness or hydrophobicity of the applied EFMs, as shown in Figure 1. Based on the statistical analysis, both EFM hydrophobicity and thickness served as equivalent variables in the control of release.

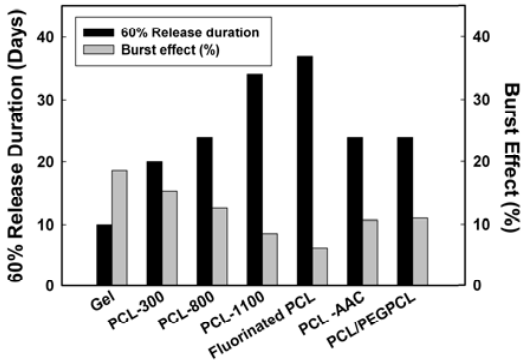

Figure 1. 60% release duration and burst effect of BSA released from composite materials comprising of EFMs with different thicknesses and hydrophobicity.

Conclusions: The combination of hydrogels and electrospun fiber mats offers a new strategy in controlled delivery. The swelling and release kinetics of hydrophilic therapeutics can be easily altered by modifying two EFM parameters: (1) thickness, which influences the drug diffusional path length and (2) hydrophobicity, which affects hydrophilic drug release by altering hydrophobic/ hydrophilic interactions between released agents and the material network. Thus, more linear hydrophilic therapeutic release profiles with smaller burst release can be obtained through the increase of either parameter.

References:

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