The Influence of Crystalline PEG on Paclitaxel Drug Release in PLGA/PEG Thin Films

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Statement of Purpose: Current atherosclerotic treatment studies require an average anti-proliferative drug dosage of 1 – 15 µg/day·cm^2. Biodegradable polyester thin films made of poly(lactic-co-glycolic acid) (PLGA), incorporated with anti-proliferative agent paclitaxel had typically slow release rates of approximately 1 µg/day·cm^2. For medical device films, a range of zero-order release rates at drug dosage of 1 – 15 µg/day·cm^2 was sought for various tissues and pathologies.

Methods: Pore forming amphiphilic compound poly(ethylene glycol) (PEG) of molecular weight of 8000 and 35,000 g/mol was incorporated respectively at 15, 25, and 50 % w/w concentrations with respect to 10 % w/w paclitaxel-loaded PLGA thin films of thickness 20 µm. Paclitaxel release rates were monitored and correlated to the release of PEG from PLGA films to further understand its role as pore forming agents and modulate drug delivery doses. Confocal Raman Spectroscopy (CRS) and Differential Scanning Calorimetry (DSC) were used to indicate homogeneity, distribution and crystallinity of the blend and its components. The mechanical properties were also assessed for its potential use as medical implants/devices.

Results: CRS mapping confirmed the co-localization of paclitaxel in the crystalline PEG phase of the phase-separated PLGA blends, seen in Figure 1. The amount of PEG released was found to be related to the level of crystallinity of PEG in the PLGA films. PEG release was also found to correlate to the release of paclitaxel, which supported the hypothesis of using a pore forming agent that phase-separates and partitions its constituents to control paclitaxel release rates.

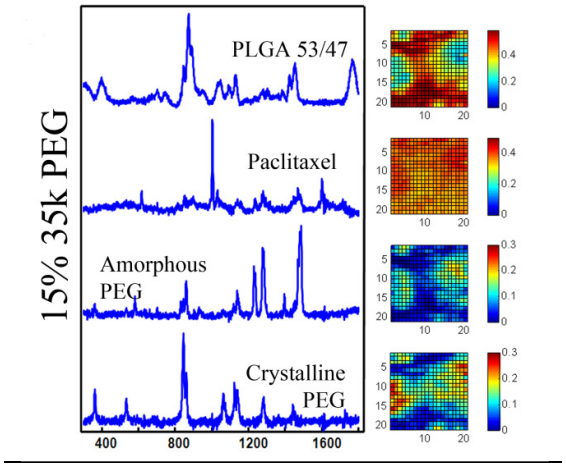

Figure 1. Confocal Raman Spectroscopy displaying paclitaxel co-localized with crystalline 35k PEG.

Two formulations have showed optimized release profiles, tensile strength, and elongation properties. For slow paclitaxel release rate, an average of 4 µg/day·cm^2 was achieved with PEG molecular weight of 35,000 g/mol at 15% w/w concentration (See Figure 2.) while a fast rate of 12 µg/day·cm^2 with PEG molecular weight of 8000 g/mol at 25 %w/w was attained for up to 12 days.

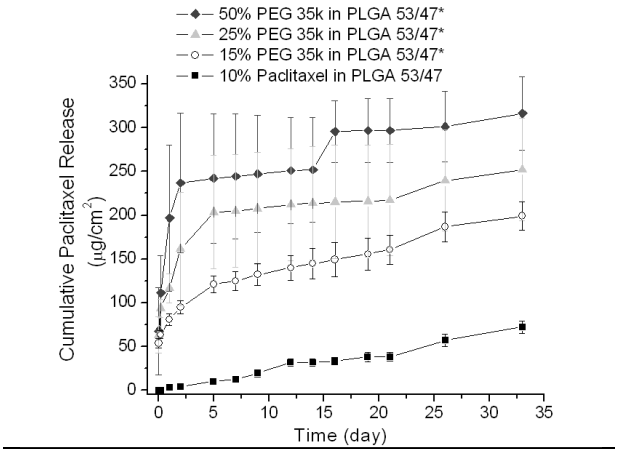

Figure 2. Release of paclitaxel from 35k MW PEG/PLGA thin films.

Conclusions: We report on the properties of PLGA films blended with a pore-forming PEG polymer. The effect of PEG molar mass and concentration of the release of paclitaxel, as well as on the mechanical properties of the PLGA films are rationalized on the basis of the nature of the PEG and its distribution within the PLGA. With CRS mapping, we confirmed the co-localization of the paclitaxel in the crystalline PEG phase of the phase-separated blends which tends to lower its tensile strength and elongation to break. Such blended films may be exploited for applications requiring enhanced, yet controlled, release rates of hydrophobic drugs from hydrophobic matrices.