Degradation and Drug Release from Poly(Ethylene Carbonate), a Surface Eroding Polymer

A. Bohr¹, Y. Wang¹, N. Harmankaya¹, J. Water¹, M. Beck-Broichsitter²
¹University of Copenhagen, ²Bayer Pharma AG

Purpose
The aim of this study was to investigate the degradation and performance of poly(ethylene carbonate) (PEC) films of different molecular weight in vitro (enzyme-triggered degradation with cholesterol esterase (CE)), in cell culture and in vivo.

Methods
PEC base material (196 kDa) was purchased from Empower Materials and further processed by thermal hydrolysis to obtain polymers of different molecular weight (i.e., 85, 110, 133, 174 kDa). Polymer films were loaded with rifampicin (RIF) or fluorescently-labeled bovine serum albumin (BSA). Samples were then characterized by gel permeation chromatography (GPC), x-ray powder diffraction (XRPD), differential scanning calorimetry (DSC) and scanning electron microscopy (SEM). In vitro drug release was examined in phosphate buffered saline (PBS) without and with added CE (0.2 mg/ml). The released RIF was analyzed using reverse phase high performance liquid chromatography and BSA was analyzed using BCA assay and a fluorescence plate reader. Degradation of films was further studied in vitro in PBS without and with CE and in cell culture (RAW 274.6 macrophages and THP-1 monocytes). Films were also implanted subcutaneously in the back of male Sprague Dawley rats and subsequently explanted and characterized at given time points.

Results
The PEC films loaded with RIF were amorphous indicating good dispersion of drug molecules in the polymer matrix. Drug release of RIF from the films showed a good correlation between polymer molecular weight and drug release rate with higher release rate observed for the high molecular weight polymers and very little release observed in absence of CE. Similarly, release of BSA from the films showed the same trend but with higher release rate observed especially in the initial phase of release. All investigated PEC films degraded via a surface erosion process (mass loss with unchanged molecular weight). The in vitro degradation studies correlated well with the observed in vitro drug release, where the PEC polymer of the highest molecular weight resulting in the fastest degradation/drug release. Further the films demonstrated similar results when incubated with a macrophage cell line or implanted subcutaneously in rats. Both in cell culture and in vivo the film degraded completely within 2 weeks indicating a rather high erosion rate. SEM analysis of film morphology showed a difference in erosion for polymers eroded in enzyme solution, in cell culture and in vivo with traces of cell mediated erosion in the two later situations. Films of different molecular weight further resulted in different pore sizes in the eroded polymer, further explaining the differences observed in degradation and drug release.

Conclusion
This study showed that PEC is an interesting polymer for controlled release purposes, and the molecular weight of this surface-eroding polymer was identified as an important parameter to control the degradation and drug release from this type of polymer.