Amino Acid Based Polyesteramides And Polyesterurethanes: Cell Responsive Matrices For Drug Delivery

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Statement of Purpose: The evolution of resorbable degradable polymers from aliphatic polyesters to nitrogen bearing polymers and eventually to amino acid based polymers such as polyurethanes, polyester amides, polyureas and polycarbonates has been accompanied with better control over degradation and release properties.
The incorporation of amino acid-based building blocks offer more than providing metabolizable building blocks, they provide one or more reactive sites that allow further modification of the polymer to tailor physicochemical properties, tune cellular response and degradation that can be either hydrolytic or enzymatic. In this paper we will utilise amino acid based polyesteramides (1) and polyesterurethanes (2) to exemplify various aspects raised by the use of amino acid based degradable polymers and their consequences on degradation and controlled release.

Methods:
Degradation studies were performed on these amino acid based polymers in phosphate buffer at 37 ^{o}C and in the presence of various enzymes such as chymotrypsin and esterases will be presented. In these studies mass loss and molecular weight determined by GPC loss as well the effect on pH was monitored.
Cell signaling studies on coatings based on the lysine based polyester urethanes where the lysine was chemically modified with arginine-glycine-aspartic acid (RGD) were performed with human foreskin derived fibroblasts with a control where cyclic RGD was introduced into the growth medium.
Drug release studies were performed on the polyesteramides and polyester urethane films with bupivacaine and dexamethasone as model drugs.

Results:
Degradation studies performed on lysine based polyester urethanes reveal that there is a lower pH drop when compared to the lactide/ glycolide based polymers of equivalent chemical structure when degradation in performed in phosphate buffer at 37 ^{o}C.

In the case of polyesteramides containing lysine and leucine, degradation is mainly enzymatic an example of the degradation profiles in the presence of chymotrypsin are given in Figure 1.

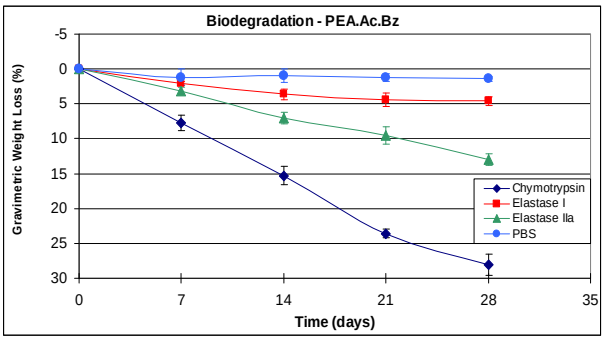

Figure 1: Degradation of polyesteramides in the presence of chymotrypsin at 37 C.

This controlled degradation has been used to control drug release as shown in Figure 2 with the bupivacaine.

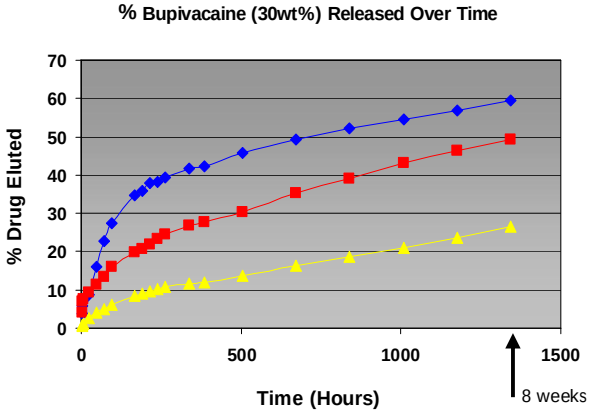

Figure 2: Drug release of bupivacaine from polyester amide films. In the absence of a top coat (diamond) and with drug loaded in a primer (square) and base coat (triangle).
Cell signaling studies on coatings based on the lysine based polyester urethanes where the lysine was chemically modified with arginine-glycine-aspartic acid were performed with human foreskin derived fibroblasts with a control where cyclic RGD was introduced into the growth medium. Preliminary results indicate that the coatings RGD modified polyester urethanes encourage fibroblast attachment

Conclusions:
Amino acid based polymers provide a means to reduce pH drop upon degradation. They can be tailored to degrade hydrolytically or enzymatically. The amino acid building block provides a moiety for attachment of anu chemical moiety for biological and cellular response.

References

1. DSM Patents: WO2007107358, WO2008055666
2. K.M. DeFife et. al. J. Biomat. Sci. 20 (2009) 1495