Novel Biodegradable Polymeric Blends for Orthopaedic Applications:

Poly[(ethyl alanato)(phenyl phenoxy)phosphazene] – Poly(lactide-co-glycolide)

Miscibility and Osteocompatibility Studies

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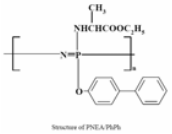
Statement of Purpose: The acidic degradation products and less than optimal mechanical performance of poly(lactide-co-glycolide) (PLAGA) due to bulk erosion have propelled researchers to develop novel biomaterials with neutral degradation products and mechanical integrity. Biodegradable polyphosphazenes are potential candidates for various biomedical applications because of their excellent biocompatibility, buffering capacity of their degradation products and synthetic flexibility[1]. We have demonstrated the feasibility to neutralize the acidic degradation products and control the degradation rate of PLAGA by blending it with ethyl glycinato substituted polyphosphazenes (EG-PPHOS)[2]. However, the low mechanical properties of EG-PPHOS make this polymer system less optimal for bone tissue engineering applications. The objective of the present study was to develop novel biomaterials by blending PLAGA with poly[(50%ethyl alanato)(50%phenyl phenoxy)phosphazene] (PNEA/PhPh) since earlier studies demonstrated good biocompatibility and mechanical performance of PNEA/PhPh[3].



Methods: PLAGA85:15 (LA:GA is of 85:15, $\overline{Mw}$ 110 kDa) was purchased from Alkermes, Inc., USA. PNEA/PhPh was synthesized via a two-step polymerization route[3]. The structure of PNEA/PhPh was confirmed by ^{31}P and ^{1}H NMR. The molecular weight of the polymer was determined by gel permeation chromatography (GPC). Blend25 has a PNEA/PhPh:PLAGA ratio of 25:75 and was prepared by mutual solvent method from tetrahydrofuran (THF). The miscibility of the resulting blend was evaluated by Scanning Electron Microscopy (SEM), Differential Scanning Calorimetry (DSC) and Fourier Transform Infrared Spectroscopy (FTIR). Primary rat osteoblast (PRO) cells were isolated from rat calvaria. The adhesion and proliferation of PRO cells on two dimensional (2D) matrices of the parent polymers and the corresponding blend were evaluated qualitatively using SEM and quantitatively via a colorimetric (MTS) assay.

Results/Discussion: The $\overline{Mw}$ of PNEA/PhPh was found to be 6,890 kDa with a polydispersity of 2.6. As shown in the SEM (Figure 1A), Blend25 formed a homogeneous blend with no visual phase separation. The miscibility of the Blend25 was further confirmed based on DSC thermogram (Table 1) where the blend showed a single glass transition temperature (T_g) intermediate between those of the parent polymers. As it is evident from FTIR (Figure 2), the C=O stretching vibrations of PNEA/PhPh and PLAGA occur at 1739 and 1750 cm^{-1}. For blend25, a second band develops at 1678 cm^{-1}. Therefore, it is assumed that PNEA/PhPh could form miscible blends with PLAGA (Blend25) via the hydrogen bonding between the secondary amine groups -N=P(NH-)-in PNEA/PhPh and carbonyl groups in PLAGA. PRO cells on Blend25 after 21 days of culture are shown in Figure 1B. Multilayers of cells could be seen on the surface of PLAGA as well as the blend. MTS result clearly shows high rate of proliferation of cells on the blend as compared to the parent polymers (Figure 3).

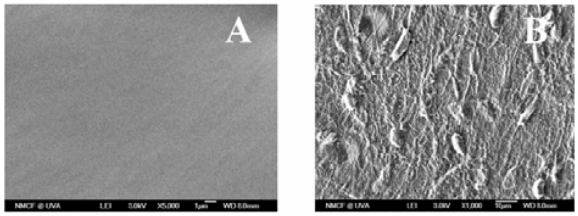


Figure 1 SEM micrographs recorded on Blend25 (A) before and (B) after *in vitro* culture.

Matrix Composition	PLAGA Content (wt%)	T_g (^{0}C)
PLAGA	100	45.4±0.8
Blend25	75	29.5±2.9
PNEA/PhPh	0	25.8±1.4

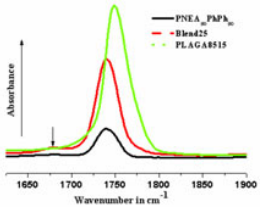


Table 1(left) T_gs of PLAGA, Blend25, and PNEA/PhPh (n=3); Figure 2 (right) FTIR spectra showing carbonyl stretching vibrations

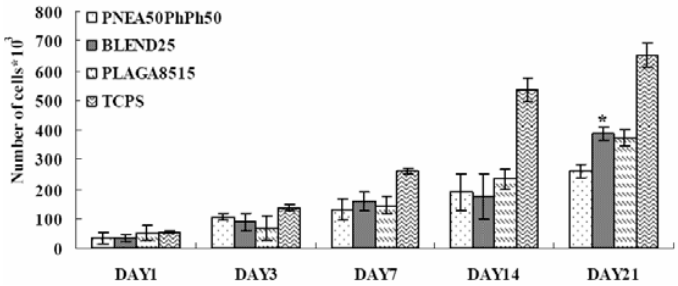


Figure 3 Cell Proliferation on 2D matrices

(*) indicates significant increase compared to PNEA/PhPh. $p<0.05$

Conclusions: We have successfully demonstrated the feasibility of developing miscible blends by blending biodegradable alanine substituted polyphosphazenes with PLAGA. The blend materials showed better *in vitro* osteocompatibility as compared to parent polymers.

References:

1. Laurencin et al., Adv Drug Delivery Rev, 55; 467 (2003)
2. Laurencin et al., Biomaterials 23; 1667 (2002)
3. Sethuraman's Ph.D. thesis; (2005)

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