

## Degradation Kinetics of Poly(lactide-co-glycolide) Mediated by Titania Nanoparticles

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**Introduction:** In the last ten years, biodegradable aliphatic polyesters, such as poly(lactide-co-glycolide) (PLGA), have attracted increasing attention for their use as scaffold materials in tissue engineering because their degradation products can be removed by natural metabolic pathways. However, one mainly concerned disadvantage about these polymers is that the degradation products of these polymers can reduce the local pH, which in turn accelerate the degradation rate and induce an inflammatory reaction at the implant sites. Therefore, it is very important to the present study to investigate the degradation behavior of PLGA influenced by dispersion of titania nanoparticles into it using ultrasonic energy at various power levels.

**Materials and Methods:** PLGA pellets (50/50 wt.% poly(dl-lactide/glycolide); Polysciences, Warrington, PA) were dissolved in chloroform and nanophase titania powder (Nanophase Technologies, Romeoville, IL) was then added to the PLGA solution to give a 70/30 polymer/ceramic weight ratio. The composite mixture was then sonicated using a W-380 sonicator (Heat System – Ultrasonics, Inc.) with output power settings at 118.75 W, 166.25 W, 213.75 W, and 332.5 W (called PTC25, PTC35, PTC45, and PTC70 respectively). After sonication, the suspension was cast into a Teflon petri dish, evaporated in air at room temperature for 24 hours and dried in an air vacuum chamber at room temperature for 48 hours.

Pure PLGA and nanophase titania compacts were used as controls. Nanophase titania compacts were prepared by dry pressing in a tool-steel die via a uniaxial pressing cycle from 0.6 to 3 GPa over a 10 minute period. The green titania compacts were then heated in air at a rate of 10 °C/minute from room temperature to a final temperature of 600 °C, sintered at 600 °C for 2 hours and were cooled down at the same rate as the heating rate. These compacts were termed sintered titania compacts (TCS).

For ceramic/polymer composite degradation experiments, initial dry substrates of interest were weighed ( $W_0$ ) and sterilized. Then, all the substrates were immersed into PBS (along with blank PBS as a reference) and were incubated under standard cell culture conditions. After 21, 28, and 35 days, specimens were removed from PBS, abundantly rinsed with deionized water to remove the soluble inorganic salt, and dried in an air vacuum chamber at room temperature for 48 hours to reach constant mass. At each time point, samples were weighed ( $W_t$ ) and the percentage of weight loss (%WL) with respect to incubation time was calculated according to the following equation.

$$\%WL = \frac{(W_0 - W_t)}{W_0} \times 100\%$$

The pH of the supernatant buffer was monitored three times a week during the experiments.

**Results:** The percentage of weight loss of PLGA was the greatest among all the substrates incubated at respective days (Figure 1). No weight loss was observed on titania compacts and glass. Among all the composites, the weight loss of PTC25 was greater than the others at 35 days of incubation. This indicated that the dispersion status of nanophase titania in PLGA played an important role in the degradation behavior of this nano-composites. Moreover, the buffering effect of titania particles in weight loss is more significant after longer time periods of incubation, which is correlated to the pH buffering effect of titania particles. Specifically, the pH drop was less than 16% for all the composites during the first 21 days of incubation. During 22 to 35 days of incubation, the pH drop was faster than the first 3 weeks of incubation.

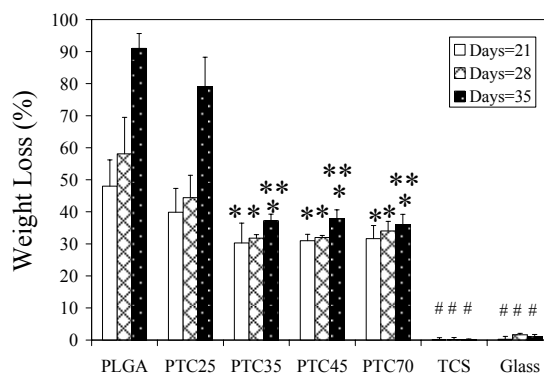


Figure 1: Percent weight loss for PLGA, PTC25, PTC35, PTC45, PTC70, TCS, and Glass incubated in PBS under standard incubation conditions. Values are mean  $\pm$  SEM; n = 3; \*p < 0.05 compared to PLGA at respective days; #p < 0.05 compared to all the composites at all days; \*\*p < 0.05 compared to PTC25 at respective days.

**Conclusions:** Data demonstrated that the dispersion of nanophase titania in PLGA decreased the degradation rate of PLGA which is considered to favor new bone growth. Our previous studies have demonstrated that dispersion of titania nanoparticles into PLGA significantly improved osteoblast (bone-forming cell) adhesion and longer-term functions (such as collagen synthesis, alkaline phosphatase activity and calcium-containing minerals deposition) [1]. In this manner, nanophase titania/PLGA composites can be promising scaffold materials for more effective orthopedic tissue engineering applications.

**References:** [1] H. Liu, E.B. Slamovich, and T.J. Webster, Journal of Biomedical Nanotechnology, 2005; 1: 83-89.