In Vitro Degradation Studies of Bioabsorbable Stents

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Statement of Purpose: Bioabsorbable stents are prepared from different types of polymers. The absorption time depends on the polymer, surface area, and additives used to prepare the stent. Bioabsorbable polymer blends can be prepared to increase ultimate strain and thereby improve the toughness of the material that can be used to prepare balloon expandable stents. The stent matrix material can be prepared from poly (lactide-co-glycolide) copolymers which are usually stiff and brittle. Elastomeric polymers added to the matrix materials can be copolymers of poly (caprolactone) and poly (glycolide). In addition to increasing the toughness values by the elastomeric polymers, the total absorption time of the stent may also be modified. The total absorption time may be reduced for poly (lactide-co-glycolide) copolymers by blending with faster degrading materials such as poly (caprolactone-co-glycolide) copolymers. This study summarizes in vitro hydrolytic degradation studies of a bioabsorbable stent.

Methods: Poly (lactide-co-glycolide) [PLGA] 85/15 used in this study was obtained from Purac. Poly (caprolactone-co-glycolide) copolymer was used in conjunction with PLGA 85/15 to provide ductility for balloon expandable stent designs. Barium sulfate, obtained from Sachtleben Corporation, was used as a radiopaque (RO) agent. Melt and solution blends of PLGA 85/15 with different amount of poly (caprolactone-co-glycolide) copolymer were prepared. Desired amount of barium sulfate was added to the formulations. Tubes were prepared from these blends with an average wall thickness of 200 µm, and were cut using excimer laser into desired stent designs. In vitro hydrolytic degradation study was conducted by placing the stents in vials filled with phosphate buffer solution at a pH of 7.4. The vials were stored in a water bath at 37°C. Stents were removed at different time points and were analyzed for changes in morphological features and molecular weight. Gel permeation chromatography (GPC) with Viscotek 270 and RI detectors was used to determine the molecular weight using chloroform as the mobile phase. In vitro accelerated hydrolytic degradation study of the stents was conducted using a titration profiler at 70°C and pH of 7.2 with 80 ml of deionized water.

Results:

In Vitro Degradation Study: Weight average molecular weight (M_w) as a function of time for melt processed stents without and with barium sulfate is summarized in Figure 1. The results show that molecular weight of the stents reduced from 240,000 g/mole to 22,000 g/mole at 10 months in the presence of 20% poly (caprolactone-co-glycolide) copolymer. There was no significant effect of barium sulfate observed in the reduction of molecular weight. The study had to be terminated at 10 months as it was difficult to collect stent samples as they became very fragile to handle for further analysis.

In Vitro Accelerated Degradation Study: Percent degradation as a function of time for solution processed stents without and with barium sulfate is summarized in Figure 2. The results show that 100% degradation occurred at 110h for stents prepared from PLGA containing 10% poly (caprolactone-co-glycolide) copolymer. The degradation time for stents containing 30% barium sulfate was 140h. Figure 2 also compares the degradation time of stents with PDS II® [poly (dioxanone)] and Vicryl® [poly (lactide-co-glycolide) 10/90] sutures available from Ethicon, Inc. Vicryl® and PDS II® sutures degrade in 50h and 140h, respectively, in these conditions. It also shows that the degradation time of the stents is between Vicryl® and PDS II® sutures.

Conclusions: A fully bioabsorbable stent has been developed by blending poly (lactide-co-glycolide) and poly (caprolactone-co-glycolide) copolymers by melt and solution processes. Two methods were developed to study the in vitro degradation behavior of the stents without and with barium sulfate. The degradation results at 37°C show that the stents are expected to fully break down in about 12-14 months. The accelerated method conducted at 70°C can be used to study the degradation behavior of stents and other medical devices in a shorter time.

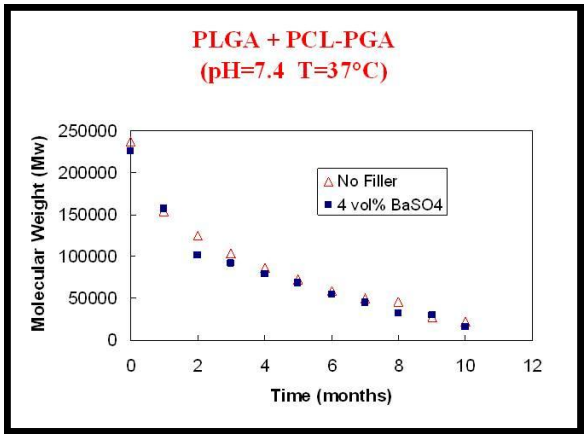

Figure 1. Molecular weight of stents without and with barium sulfate (pH: 7.4; Temperature: 37°C).

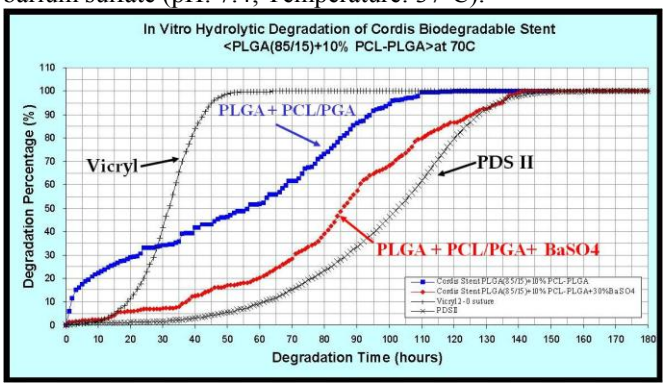

Figure 2. Percent degradation of stents without and with barium sulfate (pH: 7.2; Temperature: 70°C).