Degradation Behavior of a Resorbable Composite

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Statement of Purpose: Resorbable materials have varying degradation mechanisms. The components of the LactoSorb (85PLLA/15PGA) /Tricalcium Phosphate (TCP) composite degrade via hydrolysis and conversion to Hydroxyapaptite. The hydrolytic degradation characteristics of LactoSorb are highly dependent on the ratio of the LA ($C_3H_6O_3$) and GA ($C_2H_6O_3$). Lactic Acid has a large methyl group, which slows down the hydrolytic attack relative to the PGA which has only a hydrogen atom blocking the water molecules. Tricalcium phosphate readily converts to Hydroxyapaptite (HA) because HA is the most stable form of Calcium Phosphate under *in vivo* conditions (water and 37 ^{o}C). The purpose of this investigation is to characterize the degradation properties of the LactoSorb/TCP composite.

Methods: Injection molded cylindrical specimens of 70% LactoSorb/30% TCP Composite were exposed to *in vitro* conditions (Sorrenson's buffer at 37 ^{o}C and 47^{o}C) over clinically relevant time points. Following *in vitro* aging, the samples were mechanically tested under double shear conditions. Additionally, inherent viscosity (@ 30^{o}C, 0.25g/dL) and x-ray diffraction measurements were also conducted on the *in vitro* samples.

Results: Based on *in vitro* degradation results the Composite retains approximately 70-80% of the initial strength at approximately 8-10 weeks, and the strength approaches zero around 24 weeks *in vitro*.

The inherent viscosity profiles of the two pure LactoSorb formulations– (82PLLA/18PGA and 85PLLA/15PGA) run parallel (Figure 1). The inherent viscosity of the Composite (1.2-1.4 dL/g) starts between the pure LactoSorb formulations, however the degradation profile of the composite is more gradual and therefore the resorption is slower (Figure 1). The degradation behavior of the Composite is more gradual due to the buffering nature of the TCP. It has been found that hydrolysis rates are faster in more acidic conditions compared to neutral conditions [1].

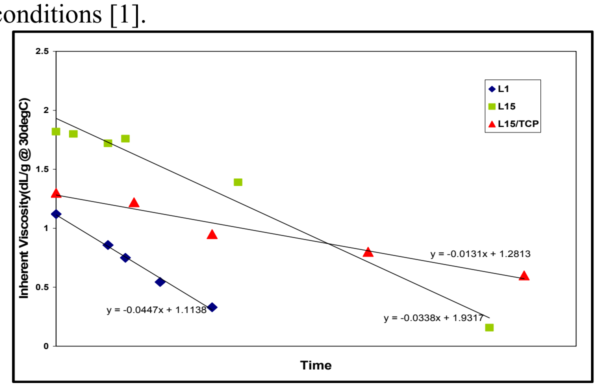

Figure 1. In Vitro Viscosity Behavior of Composite compared to 2 pure PLLA/PGA polymers

The normalized logarithmic plot of inherent viscosity was fitted with a straight line going through the origin, in accordance with first order reaction kinetics. The slope of this line was used to calculate the first order rate constants at 37 ^{o}C and 47^{o}C for polymer degradation (Figure 2). The ratio of the rate constants at 37 ^{o}C (real time) and 47^{o}C (accelerated aging) reflects the relation of the degradation profile at the select temperatures. For the Composite, the relationship is approximately 4.5, thus the rate of degradation under accelerated aging conditions (47^{o}C) is 4.5x faster than real time aging (37^{o}C). Therefore, devices can be tested under accelerated aging conditions (47^{o}C) and the degradation can be translated to real time conditions using this ratio, since it has been previously verified that the degradation of LactoSorb at 47^{o}C is only an accelerated version of the degradation at 37^{o}C with an identical chemical reaction[2].

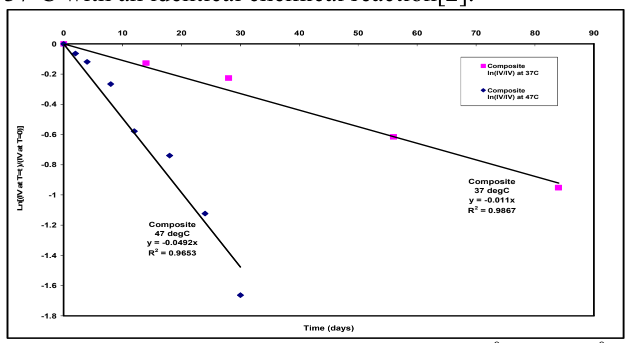

Figure 2. Rate Constants for Composite at 37^{0}C and 47^{0}C

As demonstrated by x-ray diffraction studies, the transition from TCP to HA is evident in Figure 3. *In vitro* data is plotted with TCP and HA standards. The XRD scans from the *in vitro* samples show a gradual transition from TCP to HA with time *in vitro*.

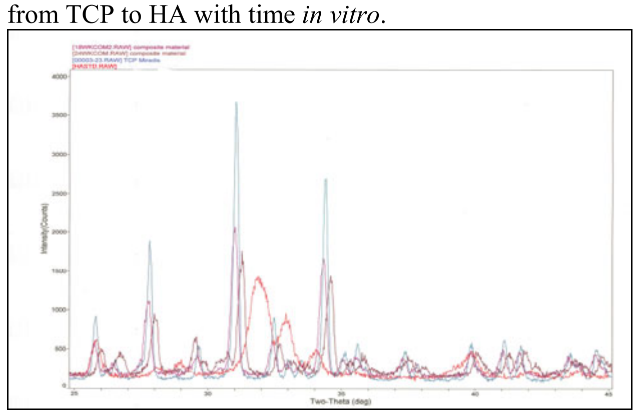

Figure 3. XRD plot of in vitro samples of ceramic phase - transitioning from TCP to HA

Conclusions: Based on the *in vitro* strength retention profile, the Composite will have 70-80% initial strength to 8-10 weeks, and the mechanical strength approaches zero around 24 weeks. Additionally, x-ray diffraction data shows a gradual transition from TCP to HA.

References: [1]T. Heya, *et.al.*, J Pharm Sci. 1994 May;83(5):636-40.

[2]M.Kumar, "Accelerated aging and hydrolysis of LactoSorb Resorbable Polymer", internal report, 2001.