Compositional Changes in vitro for Two Glycolide Based Copolymers

Ingram, D.R., Corbett, J.T., Taylor, M.S., McCullen, S.D.
Poly-Med, Inc., Anderson, South Carolina

Statement of Purpose: Polyglycolic acid and copolymers based on polyglycolic acid have been widely used throughout the biomedical device industry due to the characteristic these polymers can possess as initially strong fiber forming polymers with relatively quick resorption times.

Properties of a glycolide copolymer can be tailored to adjust strength retention, mechanical properties, and absorption characteristics by varying the structural composition (ie. random/block) and relative amounts of the constituent co-monomers (typically chosen from the following: trimethylene carbonate, ε-caprolactone, or lactide dimer).

Degradation characteristics of a material are a key indicator of biocompatibility throughout the life of a device. For this reason, a 37°C in vitro absorption study was performed to further understanding of the degradation characteristics of two glycolide copolymers in particular: Glycoprene® 6829 and Glycoprene® 935. As part of this study, HNMR analysis was performed to measure these polymer compositions post in vitro. This communication aims to present this data.

Methods: Polymer granules of Glycoprene® 6829 and 935 polymers were incubated in 0.1M/37°C/7.4 pH phosphate buffer for specified periods of time. Upon removal, samples were rinsed with deionized water and vacuum dried to constant weight.

Glycoprene® 6829 samples were dissolved in deuterated hexafluro-2-propanol (HFIP-d2). Glycoprene® 935 samples were digested into degradation products using sodium deuteroxide (NaOD) in deuterated water (D_2O). The polymer compositions were then determined by HNMR.

Results and Discussion: Compositional makeup for the in vitro hydrolyzed polymers is given in Tables 1 and 2. Polyglycolic acid, polycaprolactone, and polytrimethylene carbonate are represented by PGA, PCL, and PTMC respectively.

Hydrolysis is expected to occur at a faster rate in randomized PGA-PCL segments than in homogenous, more crystalline PGA segments, due to the higher crystallinity. Because of the higher reactivity of glycolide, homogenous PGA segments are likely to exist. The data supports the theory that homogenous PGA blocks exist, demonstrated by the increasing ratio of PGA to PCL with absorption.

PTMC increases in mol % for both of these polymers, as expected since homogenous PTMC, as present in these polymers, undergoes considerably slower hydrolysis than PGA in vitro.

The higher standard deviations observed for Glycoprene® 6829 are due lack of precision caused by broader peaks, a drawback of HFIP-d2 as a solvent. For this reason, it was decided to digest Glycoprene® 935, because the resolution of the breakdown products in D_2O is favorably more precise. Notably, while this method better satisfies this experiment's goals, structural information is lost.

Table 1. Glycoprene® 6829 composition during IVT degradation
(Analysis of Polymer in HFIP-d2)

Days IVT[A]	Polymer Composition, mol %			PGA/PCL (mol ratio)
	PGA	PCL	PTMC	
0	75.3±0.2	22.7±0.2	2.0±0.0	76.8/23.2
3	75.6±1.3	22.4±1.3	2.0±0.1	77.1/22.9
7	74.9±1.2	23.0±1.2	2.1±0.0	76.5/23.5
14	74.9±0.1	22.7±0.1	2.4±0.1	76.7/23.3
21	73.4±1.0	24.3±1.0	2.3±0.2	75.2/24.8
28	73.4±1.6	24.0±1.5	2.6±0.1	75.3/24.7
56	77.3±0.6	19.6±0.6	3.1±0.0	79.8/20.2
84	79.4±0.1	17.4±0.1	3.2±0.1	82.1/17.9

[A]n=9 for each time-point

Table 2. Glycoprene® 935 composition during IVT degradation
(Analysis of Breakdown Products in NaOD)

Days IVT[B]	Polymer Composition, mol %			PGA/PCL (mol ratio)
	PGA	PCL	PTMC	
0	93.6±0.1	4.4±0.1	2.0±0.1	95.5 / 4.5
3	93.7±0.1	4.4±0.2	1.9±0.1	95.5 / 4.5
7	93.9±0.3	4.1±0.2	2.0±0.2	95.8 / 4.2
14	94.3±0.2	3.4±0.2	2.3±0.1	96.5 / 3.5
21	94.6±0.1	3.2±0.1	2.2±0.0	96.8 / 3.2
28	94.6±0.4	3.0±0.3	2.4±0.1	96.9 / 3.1
84	94.4±0.2	2.5±0.1	3.1±0.1	97.4 / 2.6

[B]n=9 for each time-point

Conclusions: The composition of Glycoprene 6829 and 935 copolymers varies during degradation due to preferential hydrolysis of amorphous, high co-monomeric sections. This is likely to influence mechanical performance and cellular response during wound healing, thereby affecting the resulting tissue response throughout the life of the implant.

References:

[1] Shalaby, S. W., & Burg, K. J. L. (2004). Absorbable and biodegradable polymers. Boca Raton: CRC Press.

[2] Bezwada, R., Jamiolkowski, D., Lee, I., Agarwal, V., Persivale, J., Trenkabenthin, S., et al. (1995). Monocryl® suture, a new ultra-pliable absorbable monofilament suture. Biomaterials, 16(15), 1141-1148.