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Whitepaper: Polyester Degradation

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Purpose

The purpose of this research is to develop data on the hydrolytic degradation of polyesters (polylactide, polylactide-co-glycolide, etc.) and its effects on mass-loss and molecular weight reduction.

Background

Hydrolysis is the process by which an ester bond reacts with water to break into the respective alcohol and carboxylic acid. A generic sketch is shown in **Figure 1** below.

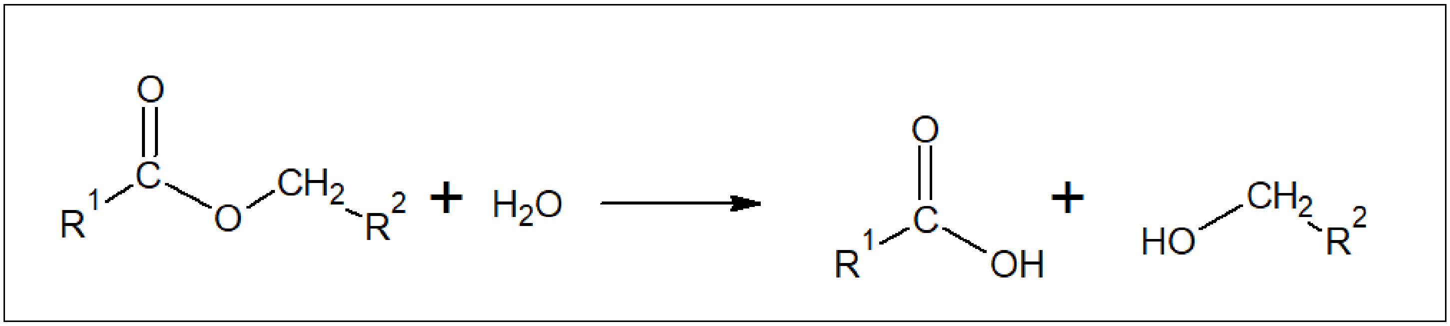

Figure 1. Ester hydrolysis generic reaction.

For alkyl polyesters (PLGA, PLA, PCL, PLCL, etc.) this reaction drives the chain-scissions along the polymer which initially decrease the molecular weight of the polymer and eventually break it down completely into water-soluble residues and oligomers. In general, polymers which present more steric hindrance to water trying to react with the backbone through either presence of methyl groups (polylactide), crystalline stacking (polyglycolide), or relatively fewer ester bonds present over the length of the chain (polycaprolactone) exhibit slower degradation than polymers which have their ester bonds relatively accessible to water. You can see more details about the mechanism and driving forces at our technical website here (http://www.lazypolymer.com/).

For this study, a series of PolySciTech catalog products were assayed for the impact of hydrolysis on their weight-content and molecular weight over the course of 9-months. This data may be useful for researchers looking to design systems with specific degradation time-lines in mind as well as for application towards drug-delivery applications.

Materials and Methods

Equipment

Water deionizer (Barnstead Easypure II)
Analytical balance (Ohaus, ± 0.1 mg)
Orbital Agitating Incubator (Southwest Science)
Waters Breeze GPC system (model 1515 isocratic pump, model 2707 autosampler, model 2414 RI detector)
Isotemp Vacuum Oven (Fisher)

Vacuum pump (Welch, Duoseal)

Reagents/Supplies
Acetone (ACE, Fisher Scientific)
Tetrahydrofuran (THF, Fisher Scientific)
Pipettor (Eppendorf)
Pipette Tips (VWR/Fisher)
Razor blades (VWR)

Polymers

The polymers tested are as shown in **Table 1**. Their initial properties, as shown on the respective manufacturing certificate of analysis, are detailed. These represent the raw, starting properties of these polymers.

Cat#	**Chemical Name/Description**	**Lot#**	**Molar Monomer ratio (LA:GA (or) CL)^1**	**Weight average Molecular weight (Mw, Da)^2**	**Number average Molecular weight (Mn, Da)^2**
AP081	Poly(lactide-co-glycolide) LG 50:50, acid endcap, (Mn 5,000-10,000 Da)	170905AHT-A	50:50 LA:GA	6933	5176
AP089	Poly(lactide-co-glycolide) LG 50:50, acid endcap (Mn 75,000-85,000 Da)	180206JSG-A	51:49 LA:GA	99,649	75,054
AP086	Poly(D,L-lactide) decanol-ester endcap, (Mn 15,000-25,000 Da)	170707ELH-A	100:0 LA:GA	33,817	16,498
AP091	Poly(lactide-co-glycolide), LG 75:25, acid endcap, (Mn 15,000-25,000 Da)	61014BPR-B	75:25 LA:GA	49,343	24,986
AP120	Poly(lactide-co-glycolide), LG 95:5, acid endcap, (Mn 10,000-15,000 Da)	70406ELH-A	94:6 LA:GA	19,459	12,740
AP136	Poly(lactide-co-glycolide) LG 75:25, acid endcap, (Mn 100,000-200,000 Da)	180112AHT-B	74:26 LA:GA	233,415	147,673
AP178	Poly(DL-Lactic-co-caprolactone), LA:CL 70:30, acid endcap, (Mn 15,000-25,000 Da)	60404JSG-A	69:31 LA:CL	38,778	18,616
AP190	Poly(lactide-co-glycolide), LG 75:25, ester endcap, (Mn 15,000-25,000 Da)	60916ELH-B	74:26 LA:GA	46,893	19,606

1. Determined by HNMR. 2. Determined by GPC-ES.

For each polymer, 100 mg was dissolved in 1 ml of acetone (10% w/v). Onto flat, level clean glass plates, 100 ul drops of this solution were pipetted and allowed to dry overnight at room temperature to yield ~ 10 mg films of each polymer. These were cut-off with a razor blade and weighed to obtain initial mass. Subsequently, each film was transferred into a tared 2 ml centrifuge tube and 2 ml of deionized (DI) water. The films were incubated at 37C with 100 RPM orbital agitation. At each time point, the water from 2 of the tubes (N=2 replicates) was pipetted away and the films were vacuum dried. The remaining film material was weighed to obtain mass and then dissolved in THF for testing by Gel-Permeation Chromatography.

Gel-Permeation Chromatography External Standard (GPC-ES)

Samples were analyzed using GPC against polystyrene standards (external standard). The GPC system consisted of Waters 1515 Isocratic HPLC pump connected to Waters 2707 Autosampler and Waters 2414 Refractive Index Detector. The detector and columns were temperature controlled at 35 ºC. GPC analysis performed by injecting 100 µL of ~ 2.0 mg per mL polymer solution dissolved in 2.0 µm filtered THF. A run time of 60 minutes was set with the flow rate of 1mL THF/min, and separation performed by a series of three GPC columns. The first two columns were Phenomenex Phenogel 5µ 300 x 7.8 mm with fixed-pore size and the last column was an Aglient Resipore 300 x 7.5 mm 3µm column. These samples were tested against Agilent Technologies EasiCal PS2 polystyrene standards lot number PL2010-0601. These standards were prepared according to manufacturer instructions using 0.2 µm filtered THF.

Results

Table 2 shows the results from this test for each indicated polymer product.

Table 2. Change in Mass, Molecular weight (Mw, Mn), and PDI (Mw/Mn) for indicated polymer over 36 weeks of degradation at 37C in water. All values represent average and standard deviation (N = 2).

Material	**Time**	**Mass Change (Wt/Wi, %)**		**Number average (Mn)**		**Weight Average (Mw)**		**Polydispersity (PDI)**	
Polymer	**Weeks**	**Average**	**STDEV**	**Average**	**STDEV**	**Average**	**STDEV**	**Average**	**STDEV**
AP089	2	99%	2%	13290	2683	23890	1324	1.82	0.27
	4	61%	20%	1998	25	2860	606	1.68	0.03
	12	4%	2%	NT	NT	NT	NT	NT	NT
	24	13%	3%	NT	NT	NT	NT	NT	NT
	36	NT	NT	NT	NT	NT	NT	NT	NT
AP081	2	48%	1%	1175	4	1497	10	1.28	0.01
	4	5%	7%	NT	NT	NT	NT	NT	NT
	12	3%	4%	NT	NT	NT	NT	NT	NT
	24	NT	NT	NT	NT	NT	NT	NT	NT
	36	NT	NT	NT	NT	NT	NT	NT	NT
AP086	2	96%	7%	14428	234	21232	245	1.47	0.00
	4	95%	3%	12365	17	21495	2802	1.71	0.27
	12	97%	1%	11180	217	21344	576	1.91	0.01
	24	89%	3%	1653	4	2815	79	1.70	0.05
	36	66%	5%	NT	NT	NT	NT	NT	NT
AP091	2	95%	1%	16841	406	25532	123	1.52	0.03
	4	88%	4%	8571	526	14936	279	1.75	0.08
	12	45%	3%	1166	22	1476	33	1.27	0.00
	24	8%	1%	NT	NT	NT	NT	NT	NT
	36	NT	NT	NT	NT	NT	NT	NT	NT
AP120	2	93%	1%	9768	1133	15695	257	1.62	0.16
	4	86%	5%	7499	429	11310	8	1.51	0.08
	12	86%	1%	2063	138	3769	264	1.83	0.01

	24	13%	1%	NT	NT	NT	NT	NT	NT
	36	NT	NT	NT	NT	NT	NT	NT	NT
AP136	2	99%	5%	71404	756	117525	1631	1.65	0.01
	4	83%	10%	27497	1160	59465	1007	2.17	0.05
	12	89%	3%	6664	392	17306	426	2.60	0.09
	24	16%	0%	NT	NT	NT	NT	NT	NT
	36	NT	NT	NT	NT	NT	NT	NT	NT
AP178	2	99%	3%	8512	1130	17058	681	2.02	0.19
	4	98%	3%	5681	518	8404	9	1.49	0.13
	12	76%	2%	1535	18	2211	27	1.44	0.00
	24	27%	2%	1400	29	2056	56	NT	NT
	36	45%	9%	NT	NT	NT	NT	NT	NT
AP190	2	97%	1%	14094	198	26287	605	1.87	0.06
	4	90%	2%	10132	1250	16679	735	1.66	0.13
	12	55%	2%	1247	31	1681	78	1.35	0.03
	24	12%	3%	NT	NT	NT	NT	NT	NT
	36	NT	NT	NT	NT	NT	NT	NT	NT

NT – Not Tested due to inadequate quantity of available material or loss of material.

The average mass-loss for each polymer is displayed in **Figure 2** below.

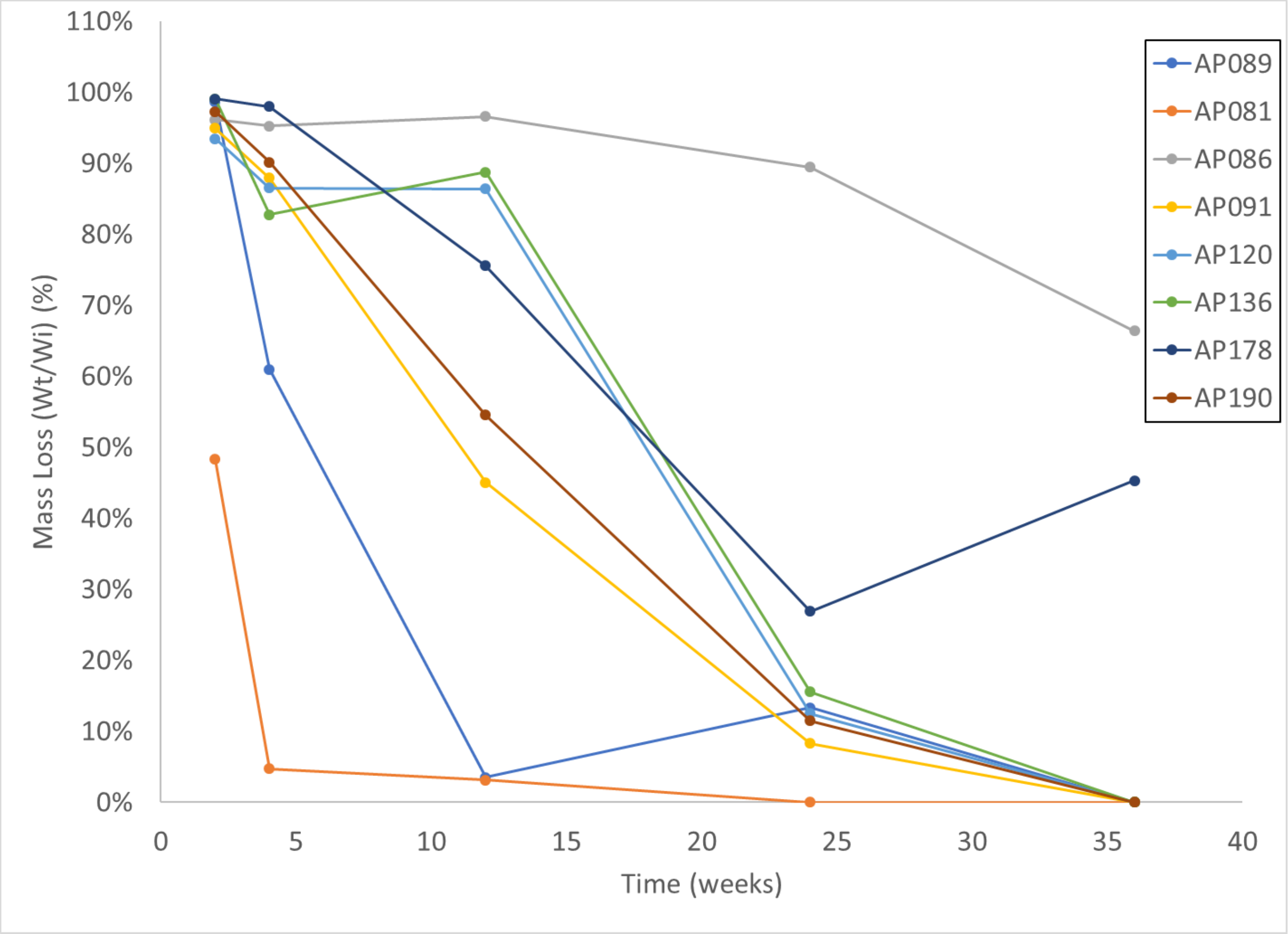

Figure 2. Mass loss of indicated polymers at each time point over the course of 36 weeks degradation at 37 °C in water.

Conclusion

The degradation profiles of these polymers vary widely based on their starting molecular weights and chemical makeup. By judiciously selecting the appropriate polymer, systems can be designed with predetermined degradation speeds in mind.