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Investigation of the thermal stability and hydrolytic degradation kinetics of poly(lactide-co-glycolide) melts

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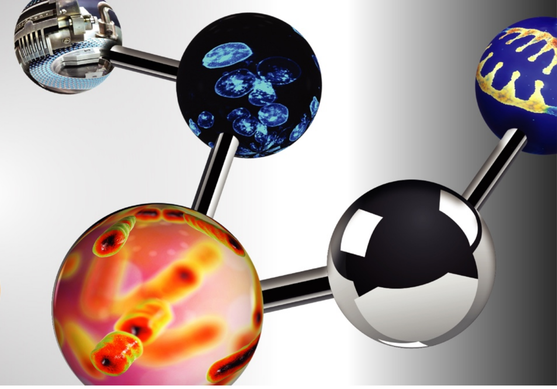

PURPOSE

Melt extrusion has been successfully applied to manufacture long-acting, biodegradable, parenteral implants based on poly(lactide-co-glycolide) (PLGA). During melt extrusion, PLGA is exposed to elevated temperatures (100–140°C) for an extended period. This research aims to investigate the effect of moisture content, polymer molecular weight, and polymer chain-end groups on PLGA stabilities during thermal processing.

OBJECTIVE(S)

1. Determine the stability of the PLGAs during melt extrusion.
2. Investigate the effects of molecular weight and chain-end groups on the degradation kinetics of PLGA at elevated temperatures.

METHOD(S)

Three PLGAs (502, 502H, and 505) with the same (1:1) lactide to glycolide ratio and **different characteristics** (i.e., end group and molecular weight) were tested in this study.

PLGA grades	Parameters from CoA		
	M_n (GPC value via PS and THF)	Inherent viscosity (dL/g)	End group
502	6880	0.20	Ester
502H	6970	0.21	Acid
505	Not available	0.73	Ester

PLGAs of various moisture contents (0.5, 0.2, and < 0.03 wt.%) were prepared.

PLGAs were held at **100 and 140°C for 10 and 30 min** in order to simulate thermal stresses during extrusion. The samples were also melt-extruded at **105°C** at **125 and 250 rpm screw speed** via a **HAAKE Minilab extruder** to evaluate their stability under shear stresses.

Study of hydrolytic degradation kinetics was conducted at **200°C with various durations (0, 10, 30, and 60 min).**

RESULT(S)

Stability

- PLGAs containing no more than 0.2% wt. water are **stable** under **common melt extrusion temperature (**100 to 140°C) for 30 min.
- PLGAs are **stable** under the extrusion barrel temperature of 105°C regardless of **screw speed** (125 to 250 rpm).

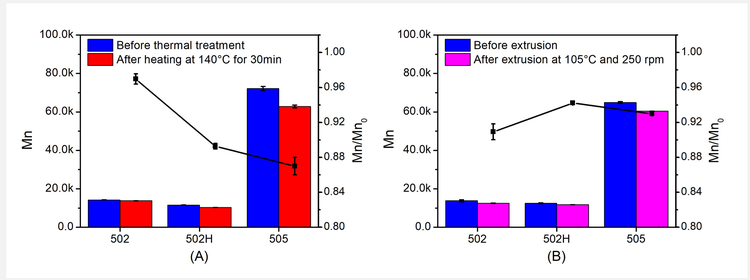

Figure 1. Comparison of number average molecular weight (M_n) between PLGA samples (502, 502H, and 505 containing 0.2% water (A) before and after thermal treatment at 140ºC for 30 min and (B) before and after extrusion at 105ºC and 250 rpm. The right y-axis represents the ratio of M_n after thermal treatment to that before(M_{n0}). Bars and symbols represent mean values, and error bars denote the standard deviation (N=2).

Degradation Kinetics

- At 200°C, PLGAs with 0.2% wt. water showed **more than a 40% reduction in M_n** within the **first 30 min** due to hydrolysis.
  - The **hydrolysis rate** of **502H** is **the highest, which is most likely** due to the presence of the **acidic end group**.
  - **505** demonstrated the **greatest M_n reduction**, as its **water to polymer molar ratio** is the highest.
- Beyond 30 min, **M_n levelled off**, suggesting the **complete consumption of water**.
- **No degradation** was observed with PLGAs containing **< 0.03% wt. water**. Instead, an **increase in M_n** was observed, which may be attributed to the **formation of macro-cycles from transesterification.**[1]
- The kinetics of hydrolysis was determined by fitting the degradation data to the model developed by Seo et al.[2]
- The **hydrolysis rate constant (k_H)** was determined by the **slope** of the fitting curve and **the initial water content (x_0).**
- With same wt.% of water, the **hydrolytic kinetics** of individual ester bond is **molecular weight independent**.

Sample	x_0 (mole/g)	k_H (mole/g min)
502	1. 111 ×10^{-4}	2.182
505	1. 111 ×10^{-4}	2.222

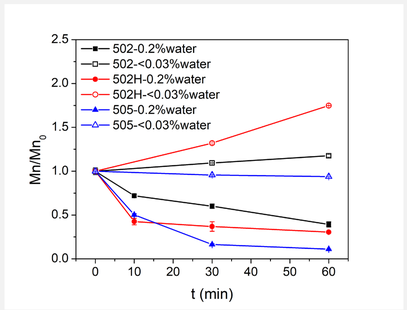

Figure 2. Molecular weight change of PLGAs samples (502, 502H, and 505) containing 0.2% (solid symbols) and <0.03% wt. (open symbols) water when thermally treated at 200ºC. Symbols represent mean values, and error bars denote the standard deviation (N=2).

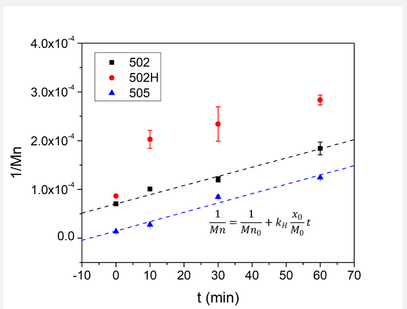

Figure 3. The reciprocal of M_n for PLGA samples (502, 502H, and 505) containing 0.2% wt. water at 200 ºC. The dashed line represents fitting curves to the kinetics model. Symbols represent mean values, and error bars denote the standard deviation (N=2).

CONCLUSION(S)

- PLGAs containing 0.2% moisture were **stable under common melt extrusion temperature** (100 to 140°C) for 10 to 30 min.
- At **200°C**, PLGAs underwent **significant hydrolysis**, and the **hydrolysis rate** was **higher** in the presence of **an acid-end group.**
- At **200°C**, the percentage **molecular weight reduction** was **greater** for PLGA of **higher molecular weight** due to the **higher water to polymer molar ratio.**
- The **hydrolytic kinetics** of **individual ester bond** was **molecular weight independent.**

REFERENCE

1. Wachsen, O.; Platkowski, K.; Reichert, K. H., Thermal degradation of poly-l-lactide—studies on kinetics, modelling and melt stabilisation. *Polymer Degradation and Stability* **1997,** *57* (1), 87-94.
2. Seo, K. S.; Cloyd, J. D., Kinetics of hydrolysis and thermal degradation of polyester melts. *Journal of Applied Polymer Science* **1991,** *42* (3), 845-850.

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