Light Scattering for the Masses™

# Polyanhydride Synthesis Techniques

Polyanhydrides are a class of biodegradable polymers used in the medical device and pharmaceutical industry as a bioresorbable carrier for drug-delivery applications. Classically, polyanhydrides are prepared by melt condensation; however, recent advances have been made in polyanhydride synthesis using a solution polymerization approach.

Gel permeation chromatography combined with refractive index and light scattering detection was used to detail differences in molecular weight and molecular weight distributions between a polyanhydride made in the melt and the same polyanhydride made by solution polymerization.

GPC analysis was performed on polyanhydride samples using a Hitachi 655A-12 pump, a Shodex SE-61 refractive index detector, and a miniDAWN light scattering detector. The mobile phase was chloroform at a flow rate of 1ml/min. and the columns included a Waters HR-4E mixed bed column. Samples were prepared by dissolving them in chloroform at ~5 mg/ml concentration, filtering through a 0.2-µm PTFE syringe filter, and injecting on the GPC through a Rheodyne manual injector with a 100µl sample loop.

Polyanhydrides, namely poly(sebacic anhydride), were prepared using melt and solution polymerization techniques and evaluated with GPC. The poly(sebacic anhydride) prepared in the melt resulted in a *maximum* weight average molecular weight of 18,940 Da with a large polydispersity index of 2.4. The solution polymerized poly(sebacic anhydride) on the other hand, resulted in a high molecular weight of 110,000 Da and a *lower* polydispersity of 1.6. As can be seen in the figures on the right, the light scattering signal for the melt polymer shows a shoulder at low retention time indicative of potential branching and other side reactions occurring during the high temperature melt polymerization, which is *not* present for the solution polymer.

Clearly, melt polymerization of sebacic acid results in a *very* different molecular weight distribution than the corresponding solution polymerization. Solution polymerization allows the achievement of higher molecular weight polymers with lower polydispersities. The higher molecular weight is preferred because it results in *better* polymer mechanical properties and the more uniform distributions lead to cleaner polymer break-down and, ultimately, a more controlled drug release.

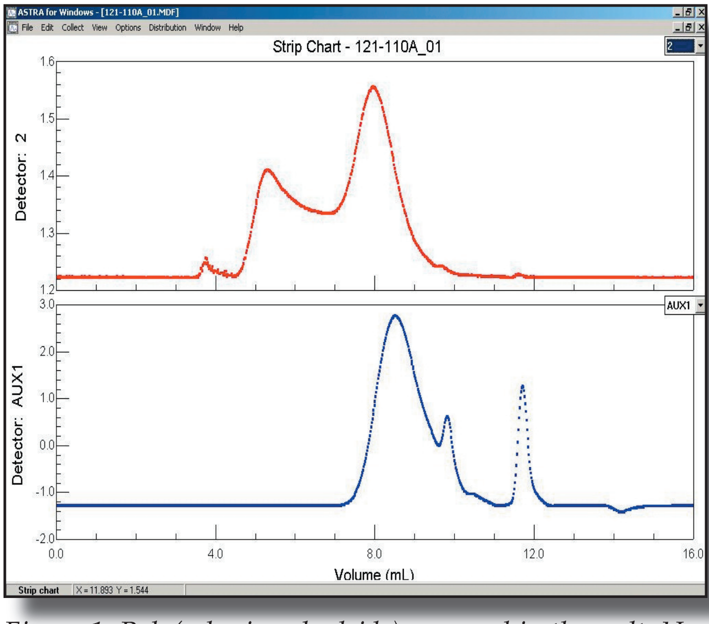


*Figure 1: Poly(sebacic anhydride) prepared in the melt; Upper chromatogram is light-scattering signal and lower chromatogram is refractive index signal.*

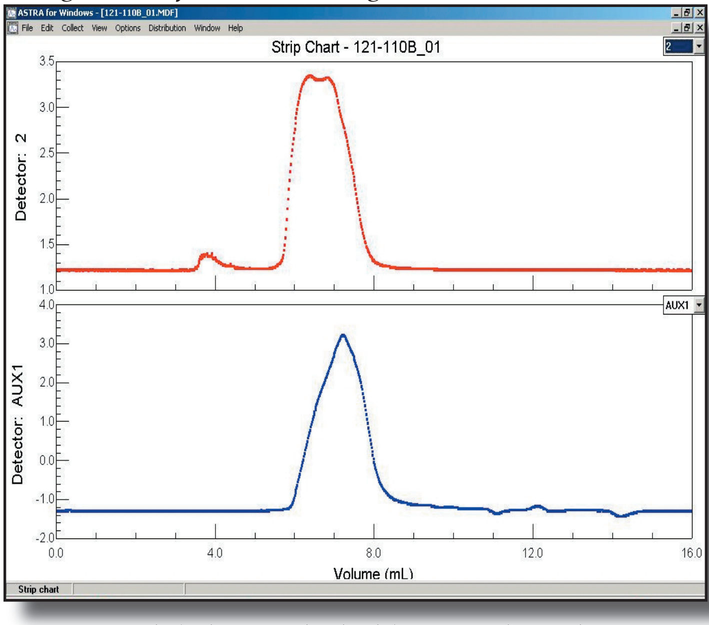


*Figure 2: Poly(sebacic anhydride) prepared in solution; Upper chromatogram is light-scattering signal and lower chromatogram is refractive index signal.*


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