Synthesis and Characterization of Polyester Nanosphones for Drug Delivery

Marc-Andre LeBlanc, David M. Stevens, and Eva Harth
Department of Chemistry, Vanderbilt University, 7210 Stevenson Center, Nashville, TN 37235

Research Directions

• Poor water solubility is a major hurdle for many promising therapeutics, preventing many drugs from being clinically accepted.
• A recent approach uses nanoparticles to encapsulate therapeutics, increasing solubility without altering the drug.
• Our research is focused on the synthesis of polyester nanoparticles, or nanosphones, formed by covalently cross-linking polymers.
• These biodegradable particles have tunable sizes based on the amount of cross-linker and can be functionalized, allowing targeted drug delivery or imaging.

Goals

• We propose a method using tin triflate, a catalyst rarely used due to difficulty removing tin from the final product.
• Our goal was to optimize this process, allowing for fast, efficient, and controlled creation of polyester polymers and nanoparticles.
• We required a method that would greatly reduce the synthesis time while maintaining a controlled linear polymerization and efficiently removing the tin.
• We specifically wanted to optimize copolymer synthesis, a process we can now control by varying the amount of solvent used in the reaction.

Copolymer Synthetic Variations

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<th>Size</th>
<th>% AVL Predicted</th>
<th>Time</th>
<th>Mn predicted</th>
<th>Mn NMR</th>
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Systematic copolymer series using allyl-l-valerolactone (AVL)

• Reactions run in bulk (not shown), standard (8.7 M) or dilute conditions (6.6 M)
• Varying solvent amount changed reaction time and AVL incorporation
• We can use this to prioritize time or material use making this a flexible synthetic pathway
• Bulk conditions finish fastest, typically under an hour, but with very low AVL incorporation
• Standard conditions provided a good balance of reaction time to AVL incorporation
• Dilute conditions are much slower, running for over 12 hours, but allow much higher AVL incorporation

Conclusions and Future Directions

We have successfully optimized the synthesis of polyester polymers for use in nanoparticle formation. Not only have we been able to reduce the synthesis time from three days to six hours, we are able to efficiently remove the tin from the product. This allows us to oxidize the polymer before finally cross-linking to create nanosphones.

With this process optimized we can now optimize the cross-linking step before testing the nanoparticles ability to encapsulate various drugs, starting with the insoluble breast cancer drug thiostrepton. Finally we will test the targeting ability of the nanoparticle in vivo.

Acknowledgements

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Harth Lab

Reference