Controlled Branching of Glycidol Polymers and Subsequent Formation of Bioconjugates with Improved Biocompatibility

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Introduction

•Nanoparticles are of great interest for transporting drugs throughout the body; however, narrow size distribution of the particles is necessary for this use. “Click” reactions have been shown to create such well-defined nanoparticles of polyester[1], and show promise with other polymers, such as polyglycidol (PG). To make PG nanoparticles using these reactions, the polymer must have a controlled level of branching, previously only available through convoluted synthetic processes involving glycidol derivatives.

•Conjugates of poly(ethylene glycol) (PEG) and proteins have been proven to improve the biocompatibility of protein drugs, improving circulation lifetime and reducing recognition by patients’ immune system.[2] Recently, polymer-protein conjugates have been prepared by grafting the polymer from the protein itself.[3] Being able to graft glycidol polymers and co-polymers from protein would allow for the creation of bioconjugates with post-modification capability and degradability without significantly decreasing the bioactivity of the protein.

Background

•Glycidol is an analogue of ethylene glycol

•Inherently hydrophilic, unlike PEG

•Ring-opening polymerization

•Linear polyglycidols

•Nanoparticles – targeted drug and biomolecule delivery

•Biomaterials

•Branched polyglycidols

•Biomolecule transport

•Smart polymers

•Post-modification possible with additional monomer

•Degradability

•Post-modification potential

•Ring-opening polymerization

Goals

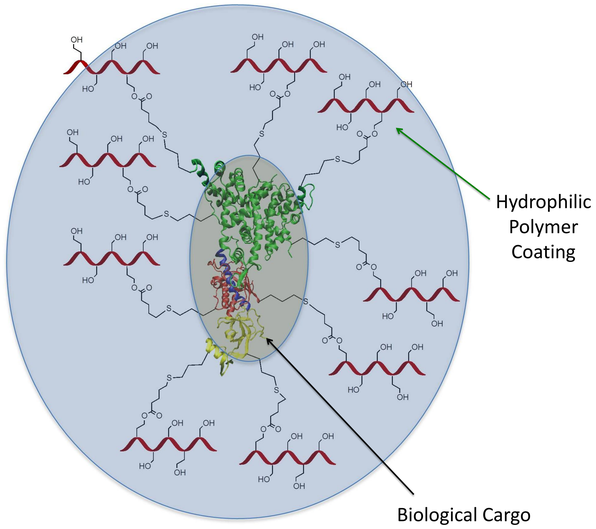
•Demonstrate kinetic control of branching

•Synthesize copolymer with post-modification capability and degradability

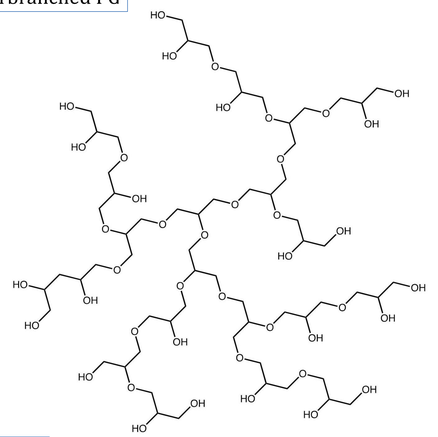
•Graft glycidol polymers directly from bovine serum albumin (BSA) protein

Bioconjugate Formation and PG Branching Systems

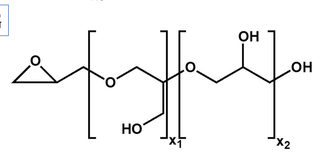
Solubilized Biological Cargo



Hyperbranched PG

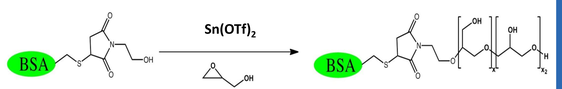


Linear PG

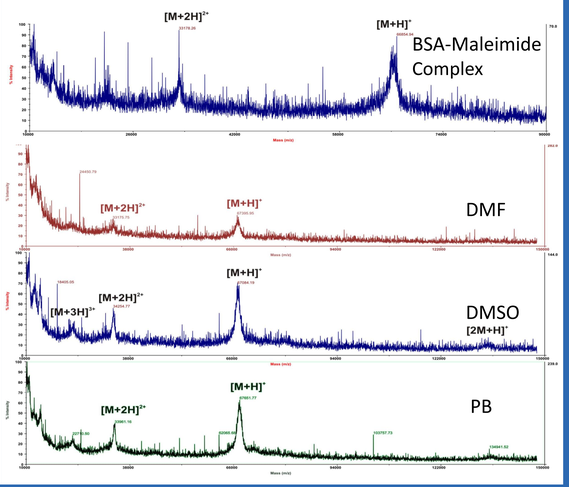


Bioconjugate Synthesis

Glycidol Grafted from BSA-Maleimide Complex



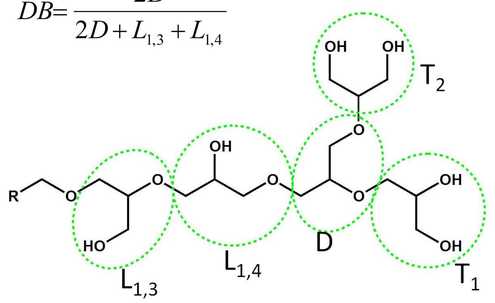
Results from MALDI



Kinetic Control of Branching

Equation to Calculate Degree of Branching

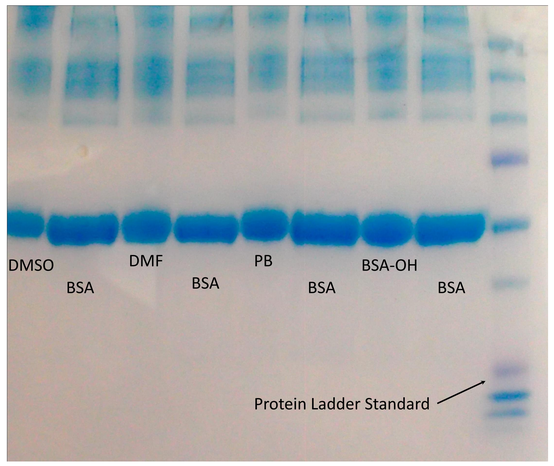
$$DB = \frac{2D}{2D + L_{1,3} + L_{1,4}}$$



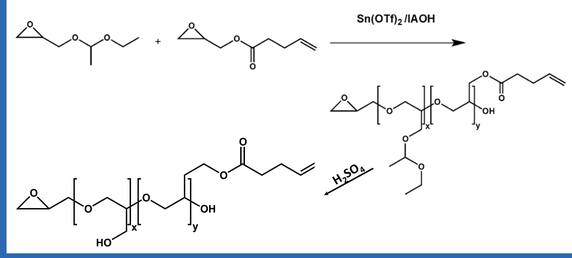
Degree of Branching from NMR Data

		Glycidol Homopolymer Temperature (°C)			
Region	**Shift (ppm)**	**25°C**	**-5°C**	**-42°C**	**-78°C**
$L_{1,3}$	81.0-82.0	1.00	1.00	1.00	1.00
D	79.5-80.5	0.78	0.41	0.35	0
2 $L_{1,4}$	73.5-74.5	3.49	4.57	5.14	5.58
2D, 2T	72.0-73.5	7.55	8.99	7.54	8.42
$L_{1,3}$, $L_{1,4}$	70.5-72.0	3.91	4.05	2.92	2.67
T	64.0-65.0	1.71	3.60	4.10	8.10
$L_{1,3}$	62.0-63.5	3.07	3.34	2.86	3.69
Degree of Branching		0.2447	0.1272	0.1142	0

Bioconjugate PAGE Results



Copolymers with Allyl Functionality



Conclusions

Polyglycidol was successfully grafted from BSA, as shown by MALDI and PAGE. Also, the degree of branching of polyglycidol was successfully kinetically controlled. Future work will focus on the effect of controlled branching of the polyglycidol on the bioactivity of BSA.

Acknowledgements

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References

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