Derivatization of Polyglycidol and Synthesis of Hydrogels by Oxime Click Chemistry

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Abstract

A hydrogel is a network of hydrophilic polymers that has the ability to absorb water. These gels have similar properties to human organs and tissues, and thus have many medical applications, such as drug transport and gene therapy. These hydrogels can act as a matrix to which biomedical nanoparticles can be attached and allow drugs to be more effectively delivered throughout the human body.

This project focused on the synthesis of semibranched polyglycidol hydrogels by functionalizing polyglycidol polymers and reacting these various derivatives with each other to form hydrogels. Semibranched polyglycidols are a new class of polymers discovered in 2012 to replace PEGylated components in proteins and hydrogels. Three different polyglycidol building blocks were synthesized : amino-oxy polyglycidol, thiol polyglycidol, and allyl ester polyglycidol. In order to characterize the properties of the derivatives that were synthesized, model reactions were conducted using 3-ethoxy-1,2-propanediol because it has similar functional groups to polyglycidol.

The three buidling blocks carry critical functionalities for hydrogel formation with polyester and polycarbonate derivatives. These functionalities are essential in the preparation of innovative degradable hydrogels that are injectable or formed outside of the biological system.

Background

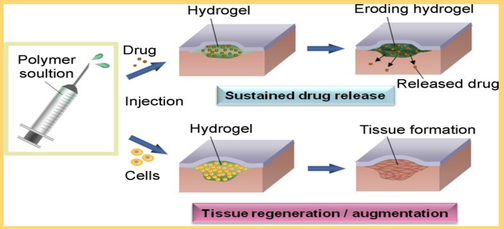
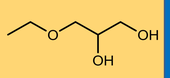


Figure 1: Diagram showing two of the possible uses of hydrogels: drug release and tissue regeneration. Hydrogels can act as a matrix for both large macromolecules and cells by increasing their solubility in the human body.

Project Goals

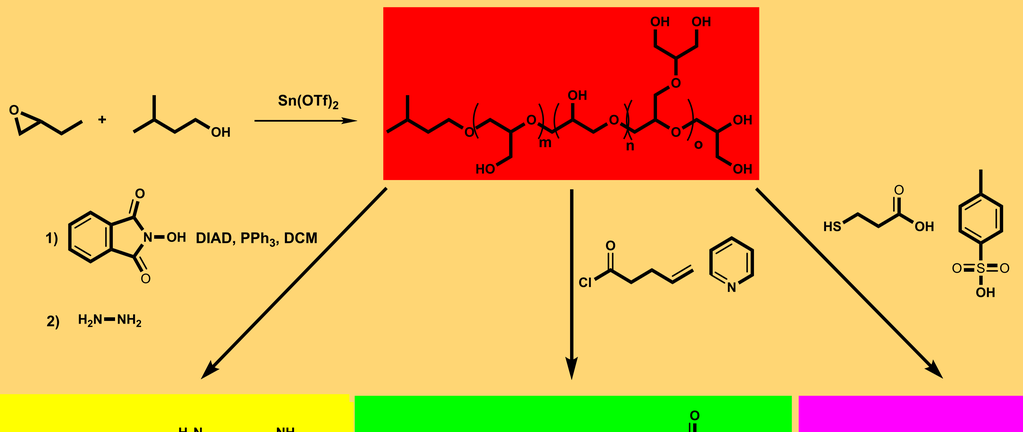
- Functionalize the hydroxyl groups on polyglycidol to form three different functionalized derivatives.
- Determine the reactivity of primary and secondary hydroxyl groups by conducting model reactions with 3-ethoxy-1,2-propanediol
- React one of the functionalized polymers to form hydrogels in pilot study
- Test hydrogels for their ability to swell and degrade.

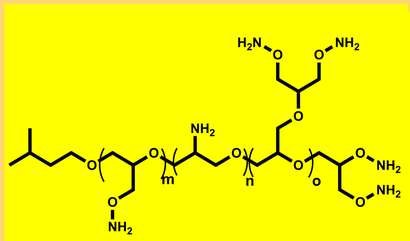


3-Ethoxy-1,2-Propanediol

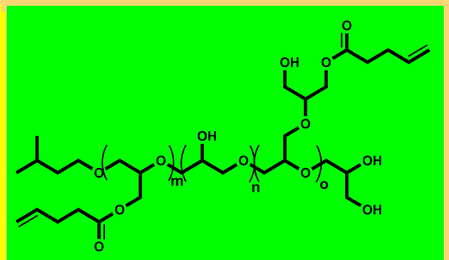
Synthesis of Polyglycidol and Functionalized Polyglycidol Building Blocks

Developed Semibranched Polyglycidol

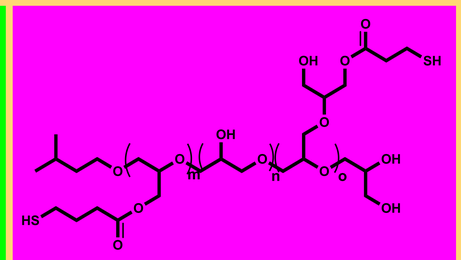




Aminooxy Polyglycidol

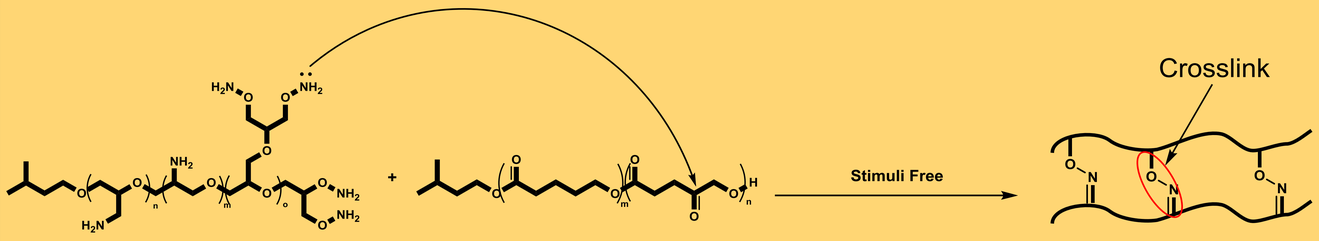


Allyl Ester Polyglycidol



Thiol Polyglycidol

Synthesis of Polyglycidol Hydrogels by Oxime Click Reactions



Aminooxy Polyglycidol

OPD / Valerolactone Polymer

Hydrogel

Image 1: Hydrogel Composed of Amino-oxy Polyglycidol and OPD/VL Polymers

Characterization

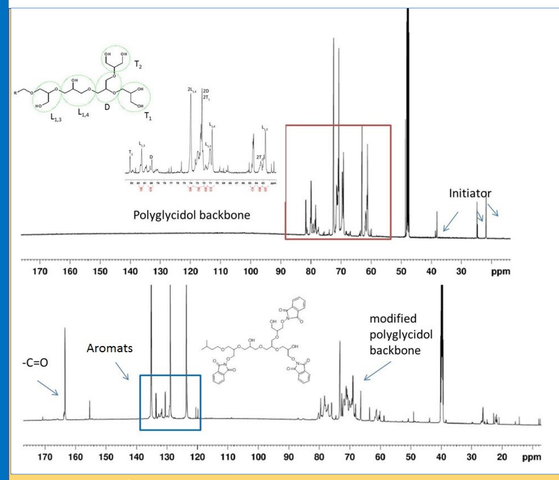


Figure 2: ^{13}C NMR of polyglycidol (top) and protected aminooxy polyglycidol (bottom).

Conclusions & Future Research

This project was successful in synthesizing novel semibranched polyglycidol to function as a smart PEG alternative and then derivatizing it into three different polymers with amino-oxy, allyl ester and thiol functional groups. All structures were fully characterized by ^{1}H NMR and ^{13}C NMR to confirm their degree of functionalization, which was either 20% or 40% of the hydroxyl groups present in the polyglycidol precursor. Model reactions showed that primary OH groups are preferentially functionalized.

These building blocks can now be used as reaction partners in polyglycidol-based hydrogels by click reactions in a similar manner to the aminooxy polyglycidol and OPD / valerolactone polymer hydrogel we synthesized and can further optimize.

Ongoing Studies Include:

- Swelling tests to determine the hydrophilicity of each gel and their abilities to absorb water.
- Degradation tests to determine the biodegradability of each gel.
- Cell Culture assay tests to determine the biocompatibility of each gel and incorporation of biological structures
- Structure – Property Relationship (SRP) of the functionalized polyglycidols regarding their degree of functionalization and how these varied percentages will affect the properties of the gel.

References & Acknowledgments

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Grover, G.N.; Lam, J.; Nguyen, T.H.; Segura, T.; Maynard, H.D. *Biomolecules*, **2012**, 13, 3013-7.
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