In-vitro material characterization of ROS-responsive poly(thioketal) polymeric scaffolds for treatment of chronic wounds

VANDERBILT UNIVERSITY

Caylee Marshall[1], Prarthana Patil[2], Craig Duvall[2]

1 Department of Chemical Engineering, University of Kentucky

2 Department of Biomedical Engineering, Vanderbilt University

UNIVERSITY OF KENTUCKY College of Engineering

Abstract

Chronic wounds affect millions of Americans each year. There are currently limited and inefficient treatment regiments which augment wound healing. The use of degradable biomaterials, such as foams, is being extensively studied for the treatment of chronic wounds. These wounds are characterized by poor vasculature and elevated levels of reactive oxygen species (ROS). Our motivation is to leverage elevated ROS levels as a stimuli for the degradation of poly(thioketal) urethane (PTK-UR) scaffolds. We have previously fabricated urethane foams using two component liquid reactive molding by using tri-functional isocyanates and mercaptoethylether (MEE) PTK diol[1]. Nonspecific degradation of polyester urethane foams can be eliminated by using ROS degradable PTK-UR chemistry to augment formation of granulation tissue and decrease fibrosis. This project has focused on making increasingly hydrophilic polymeric PTK diol components to decrease immunogenicity and increase clearance of scaffold degradation products.

Background and Approach

Chronic Wounds:

6.5 million people in the US have non-healing wounds.

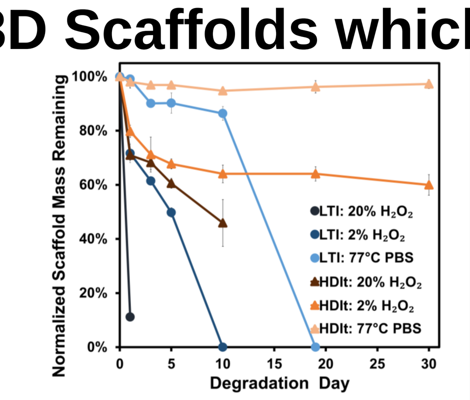
It cost $25 billion dollars annually to treat these wounds.

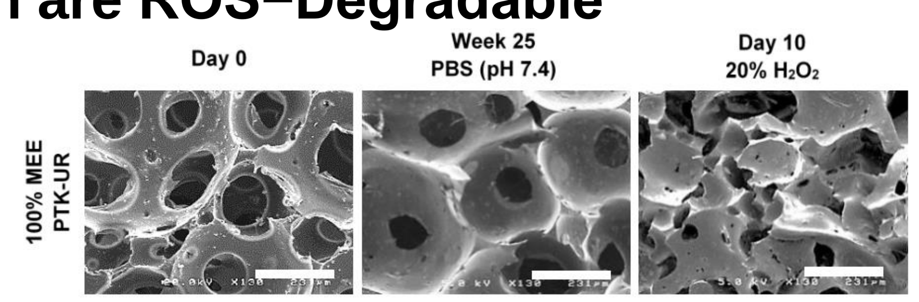
If they are unable to be treated, it can result in amputations.

Current Standard of Care: Regranex

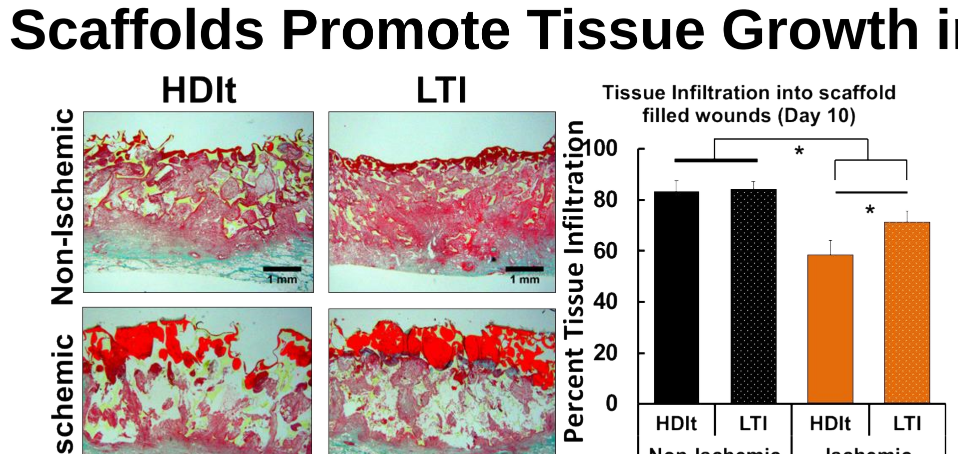
- Platelet derived growth factor delivery
- Only 50% achieve wound closure

PTK Diols Combine with Isocyanates to form Porous 3D Scaffolds which are ROS−Degradable[1]





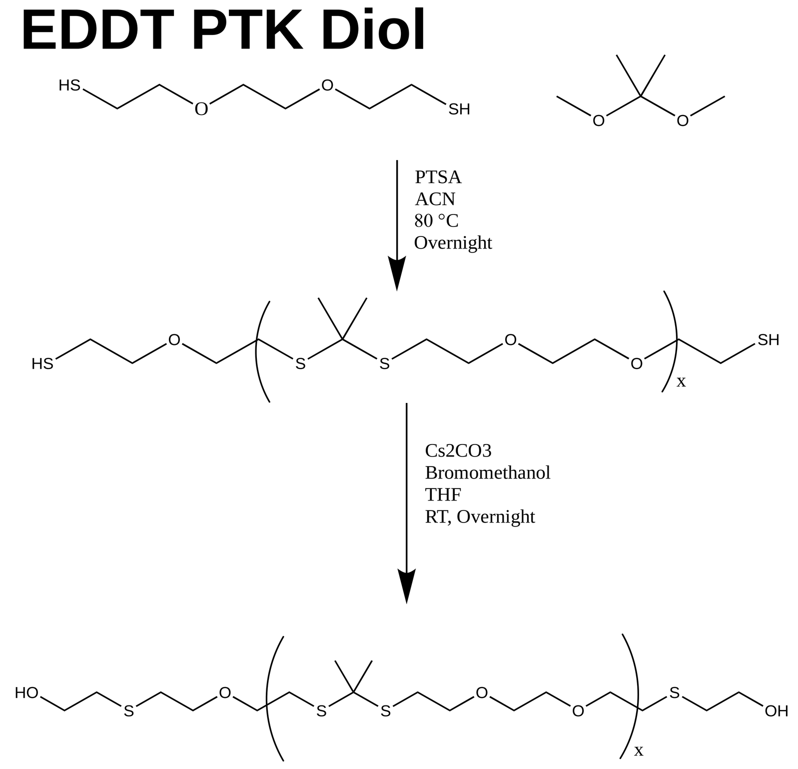
PTK-UR Scaffolds Promote Tissue Growth in Pigs[3]



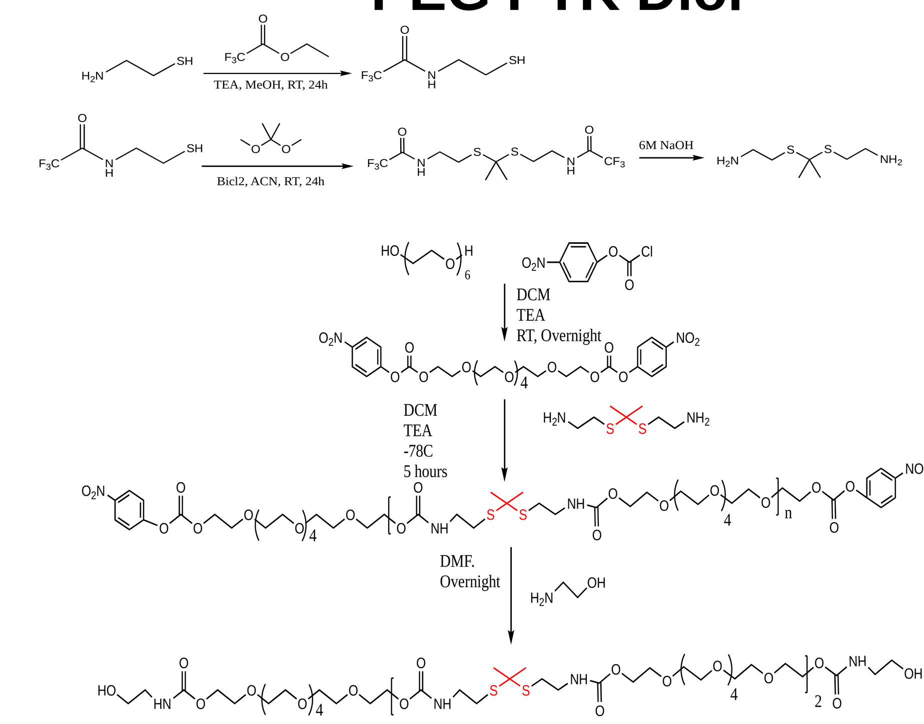
Results

Synthesis of PTK Diols

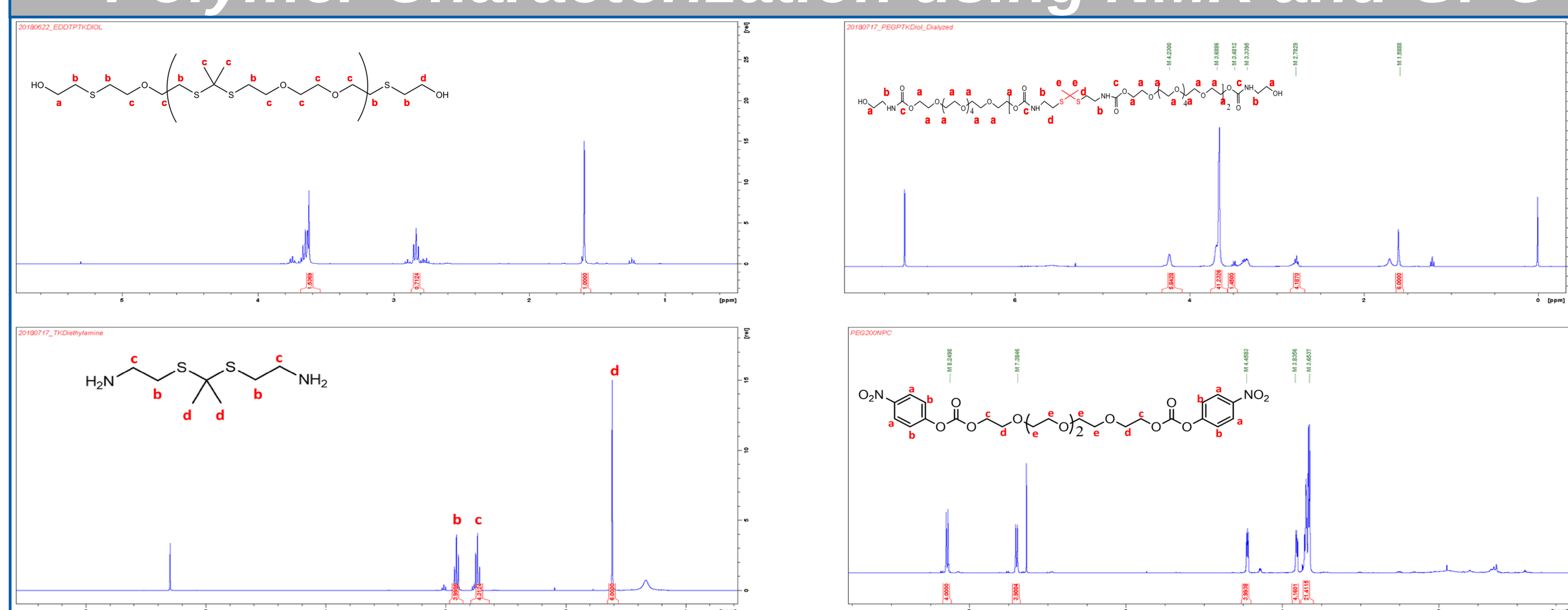
EDDT PTK Diol

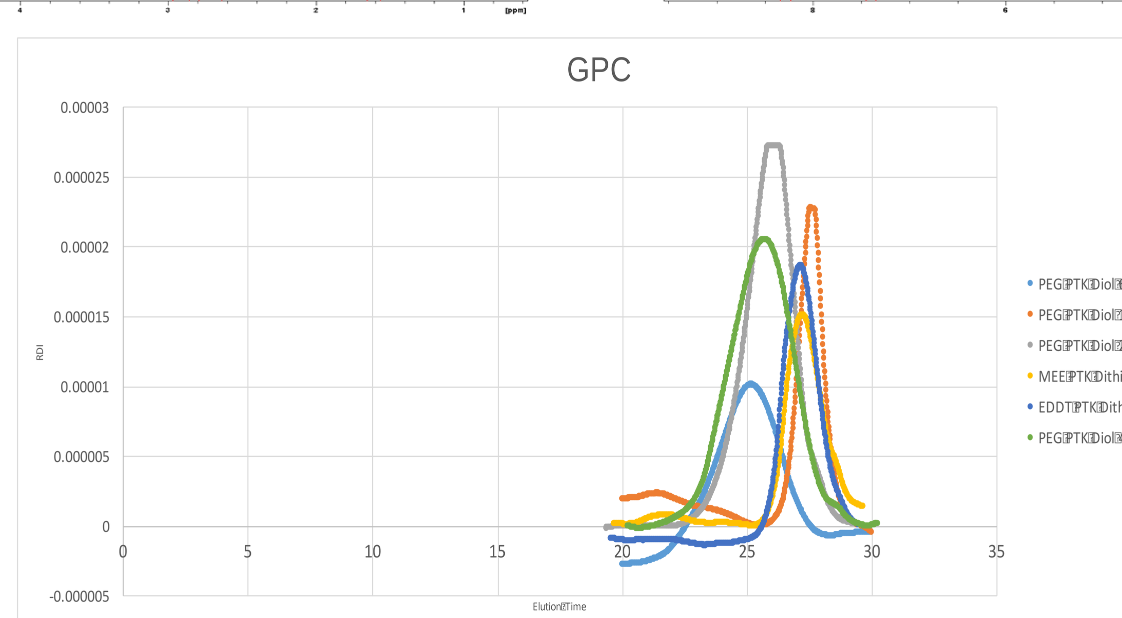


PEG PTK Diol

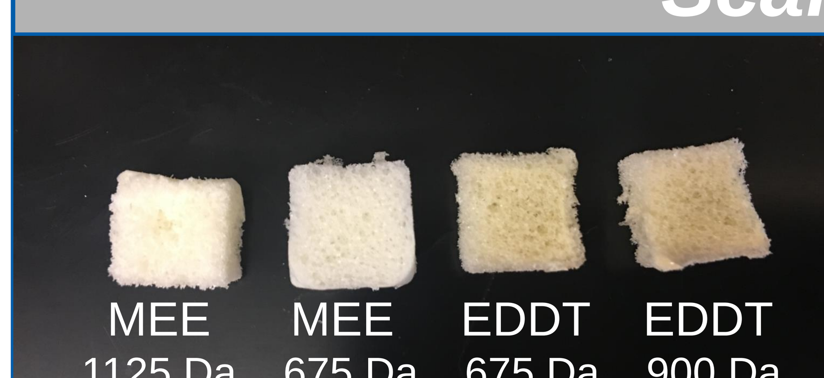


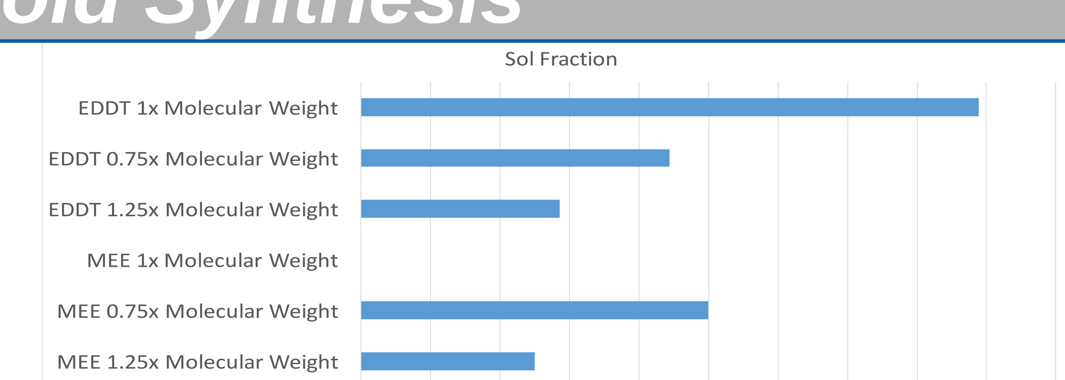
Polymer Characterization using NMR and GPC





Scaffold Synthesis





In order to determine which optimized foam to use, sol fraction was determined. Sol fraction = $\frac{\text{Original Mass} - \text{Swollen Mass}}{\text{Original Mass}} \times 100$. MEE 900 Da and EDDT 1125 Da were the two formulations chosen to do further testing with. The EDDT 1125 Da was further optimized to lower the sol fraction.

Future Work and Conclusions

- Successfully synthesized EDDT PTK diol and PEG PTK diols
- Confirmed chemical structures of different diols using NMR and GPC
- Fabricated PTK-UR foams

Future Work

- Mechanical testing using DMA and DSC
- Degradation studies in oxidative media
- In-vitro cytotoxicity testing
- Application of PTK-UR scaffolds in larger animal models to study tissue response

ROS degradable, polymeric scaffolds are a possible option as a treatment for healing chronic wounds. Further testing would be necessary to determine the extent to which the scaffolds would increase cellular infiltration and wound healing.

References

1 Martin et al, *A porous tissue engineering scaffold selectively degraded by cell-generated reactive oxygen species*, Biomaterials, 2014

2 Martin et al, *Local Delivery of PHD2 siRNA from ROS-Degradable Scaffolds to Promote Diabetic Wound Healing*, Advances Healthcare Materials, 2016

3 Patil et al, *Porcine Ischemic Wound-Healing Model for Preclinical Testing of Degradable Biomaterials,* Tissue Engineering Part C: Methods, 2017

4 Sun et al, *Advances in skin grafting and treatment of cutaneous wounds*, Science, 2014

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