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Material and Structure Design for Anti-HIV Drug Delivery Devices using FFF 3D Printing

PLA:PEG copolymer blends with TDF

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Collaboration with Dr. Jill Steinback and Kevin Tyo

University of Louisville

IMPACT Research Experience for Undergraduates

Award ID 1560235

National Nanotechnology Coordinated Infrastructure

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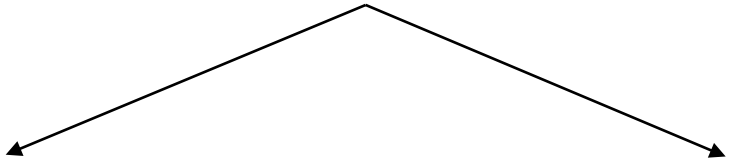
Summary of Project

The goal of this project is to 3D print intravaginal rings using a blend of polylactic acid (PLA) and polyethylene glycol (PEG) infused with TDF, an anti-HIV medication.

Factors of Drug Delivery



Materials

- Biocompatibility
- Tuned Degradation
- Mechanical & Physical Integrity and Strengths

3D Structure

- High Surface Area
- Tuned Structure Disintegration
- Complex Architectures

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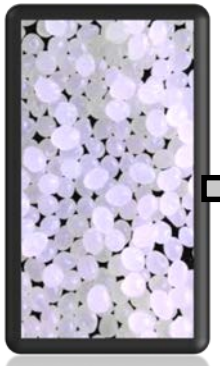
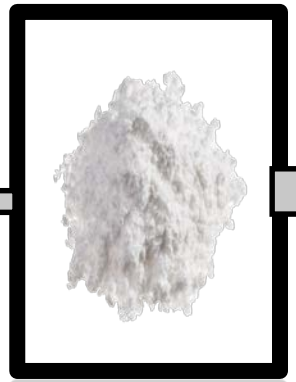
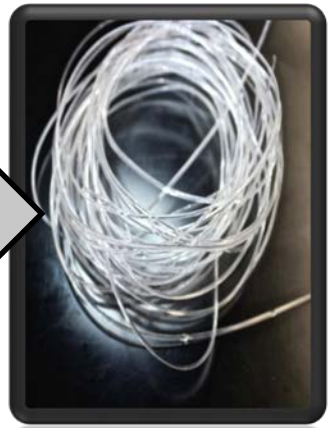
Experimental Approach



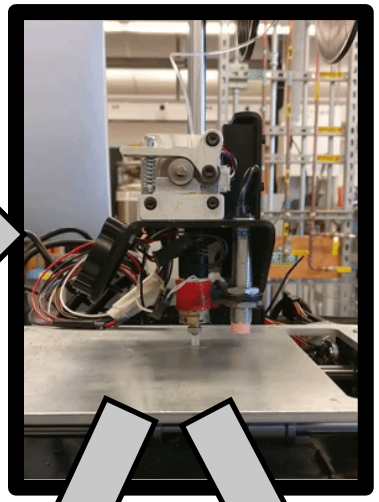


TDF is combined with the 90:10 polymer blend

Blend extruded into filament



Filament used on Simplebot Printer to print devices



4mm x 8mm cylinders and 15mm x10mm pucks used for device testing

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Materials Being Tested

- 50:50 PLA:PEG copolymer can be blended with PLA to make unique materials with varying degradation rates.
- Based on previous testing, we studied the degradation of 90:10 PLA:PEG for optimal release time

PLA/PEG Ratio	PLA percent	Copolymer percent
50/50	0%	100%
75/25	50%	50%
90/10	80%	20%

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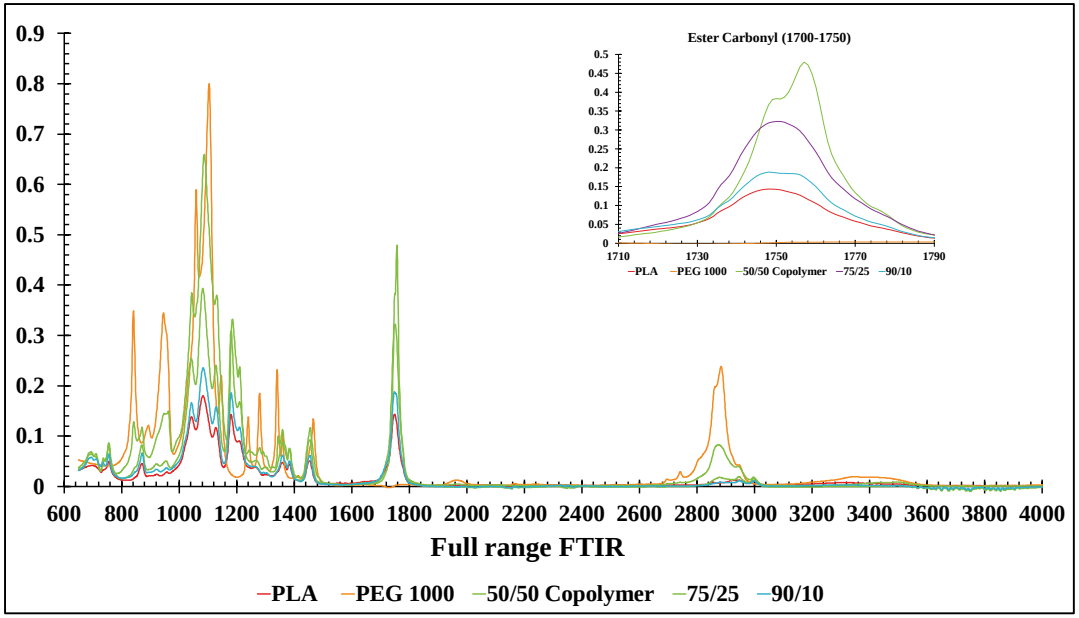
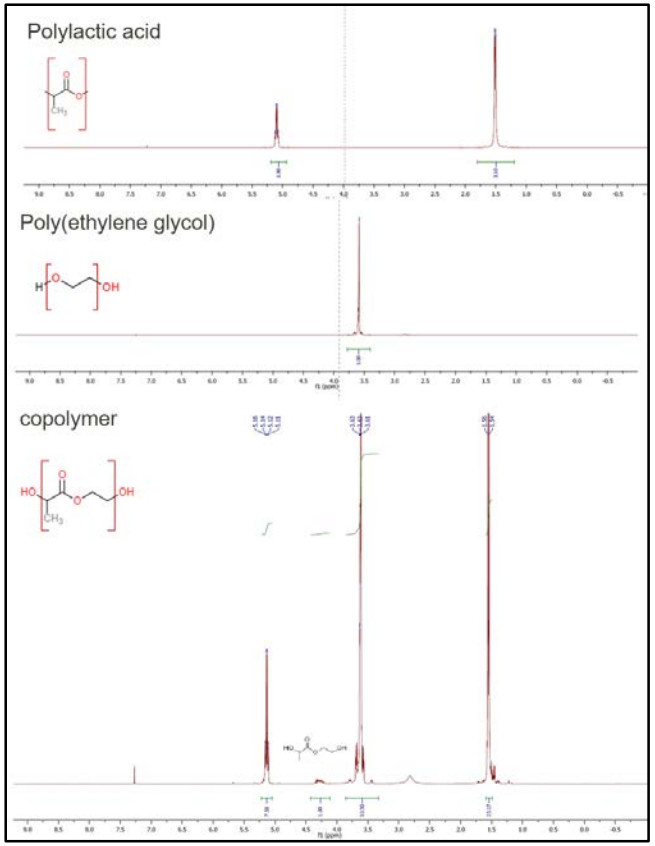
Copolymer Confirmation



Copolymer formation confirmed by the disappearance of the –OH stretching around 3400 cm^{-1} and also monitoring the C=O stretching around 1750 cm^{-1}



NMR showing equivalent integration of peaks

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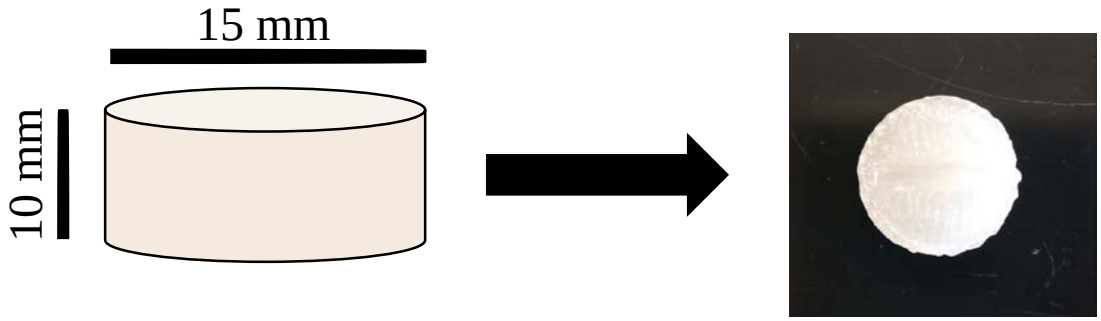
Degradation Testing

- 90:10 PLA:PEG pucks were 3D Printed and Injection Molded.
- Each were dissolved in Phosphate Buffered Saline (PBS) according to the following times: 4, 6, 12, 24, 96, 168 hours
- UV-Vis and Weight loss were used to compare the two manufacturing methods



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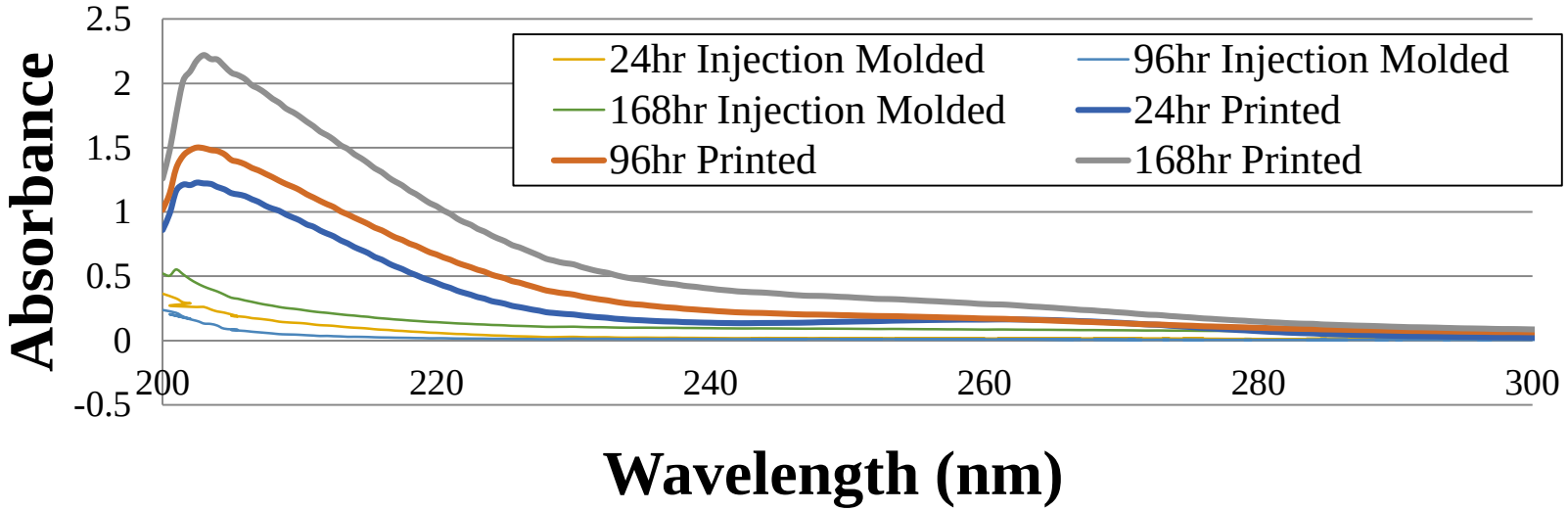
Comparison of 3D Printed and Injection Molded Materials

UV-Vis of 3D Printed and Injection Molded Pucks



3D Printed and Injection Molded pucks were tested for degradation and compared using weight and UV-Vis

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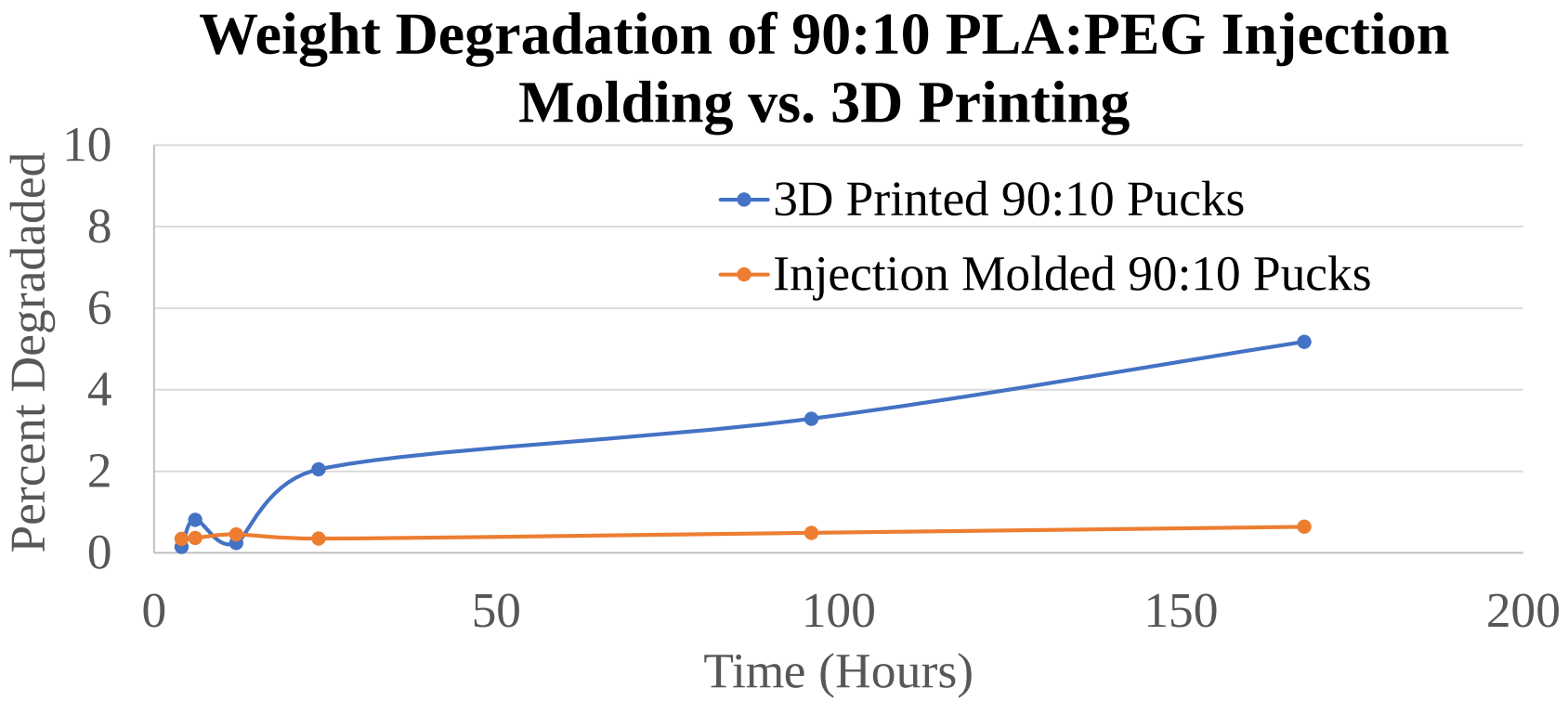
Comparison of 3D Printed and Injection Molded Materials



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Device Design

- Three different devices were designed with increasing surface area to test degradation
- These devices were each 4mm x 8mm cylinders to be used for later testing in mice

Final batches of each device

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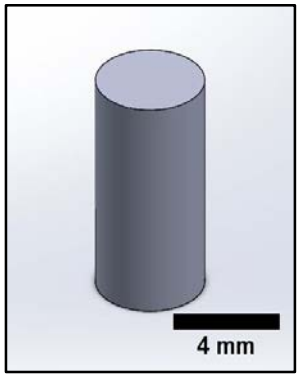
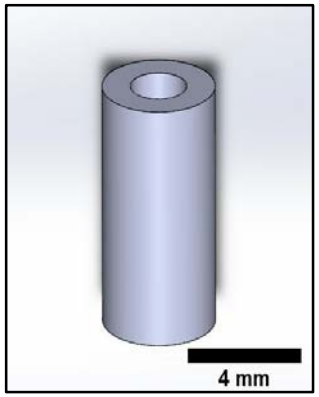
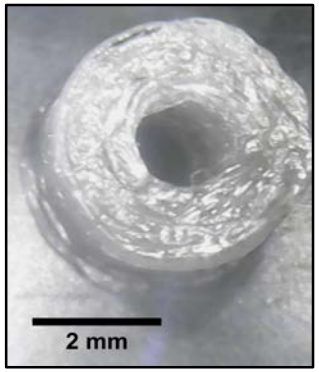
Drug Delivery Devices

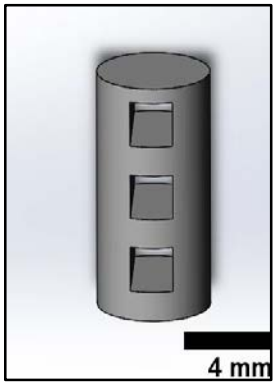


Device 1
Surface Area: 125.6 mm





Device 2
Surface Area: 169.7 mm



Device 3
Surface Area: 180.3 mm

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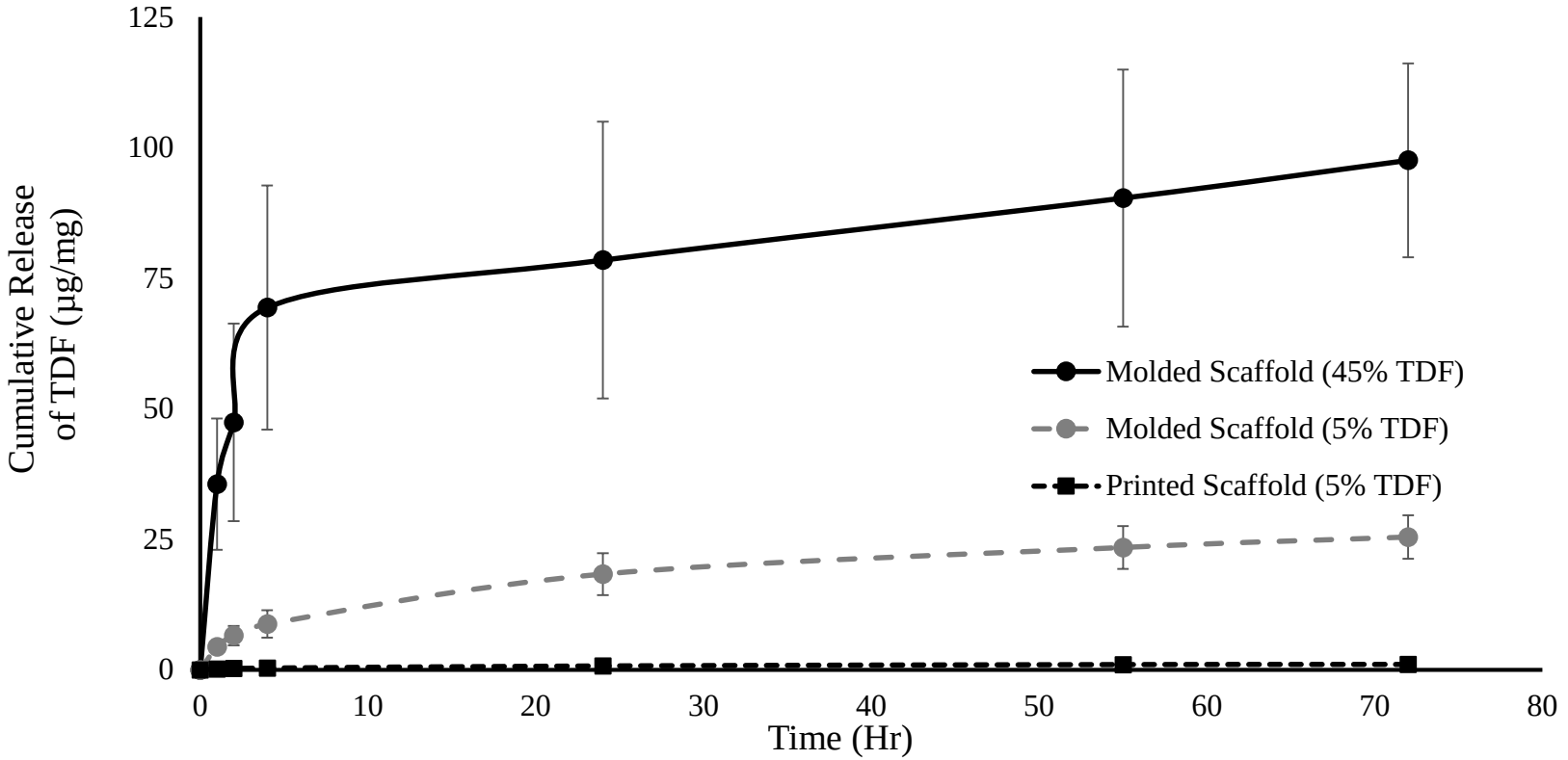
Cumulative Release Testing



Crushed scaffolds were tested in simulated vaginal fluid. Pockets of TDF in the molded scaffolds likely account for the better release than the printed scaffold.

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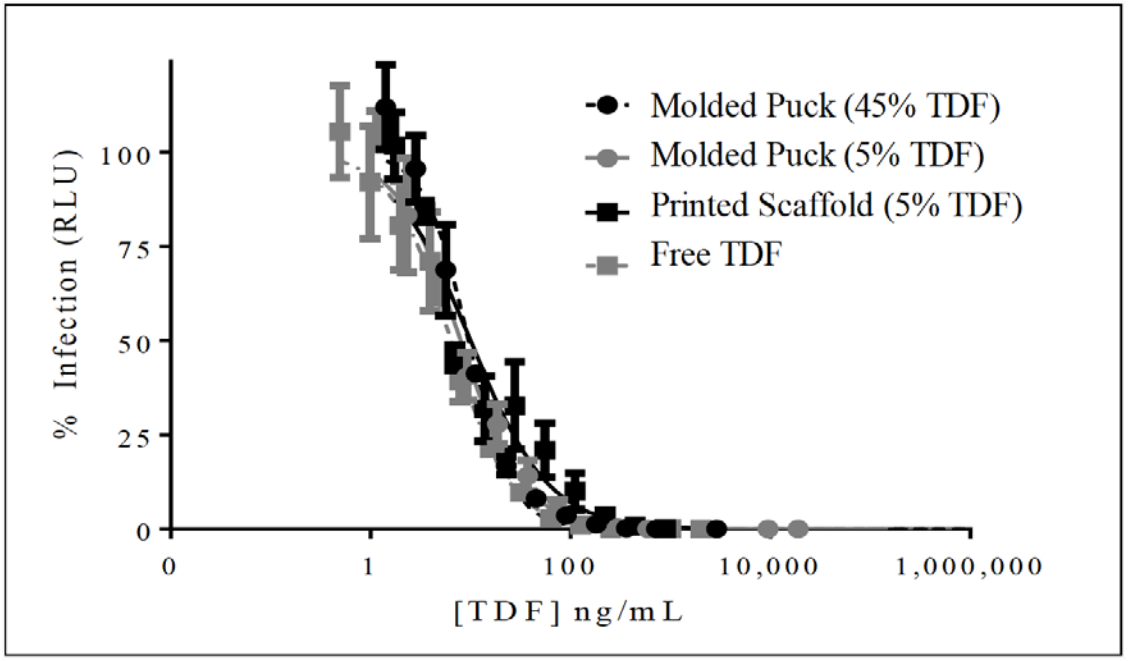
Percent Inhibition



HIV Inhibition Assay Results	
Formulation Name	**IC_{50} (ng/mL)**
Molded Puck (45% TDF)	9.5 ± 1.8
Molded Puck (5% TDF)	7.9 ± 1.8
Printed Scaffold (5% TDF)	10 ± 1.9
Free TDF	6.4 ± 1.8

IC_{50} indicates the concentration of drug that eliminated 50% of the virus. The values of the scaffold compared to Free TDF are within reason of one another, each having overlap.

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Conclusions

- Unique biocompatible and biodegradable polymeric devices were designed and developed using 3-D printing approach with low-cost commercial printers

- Degradation studies in PBS indicated the higher porosity of 3D printed materials allows for better degradation than injection molded materials

- Customized 3-D printed devices can be designed and developed for use of controlled degradation in drug delivery systems for HIV prevention

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Acknowledgements

- Dr. Kunal Kate
  (University of Louisville)

- Atre/Kunal Lab Group

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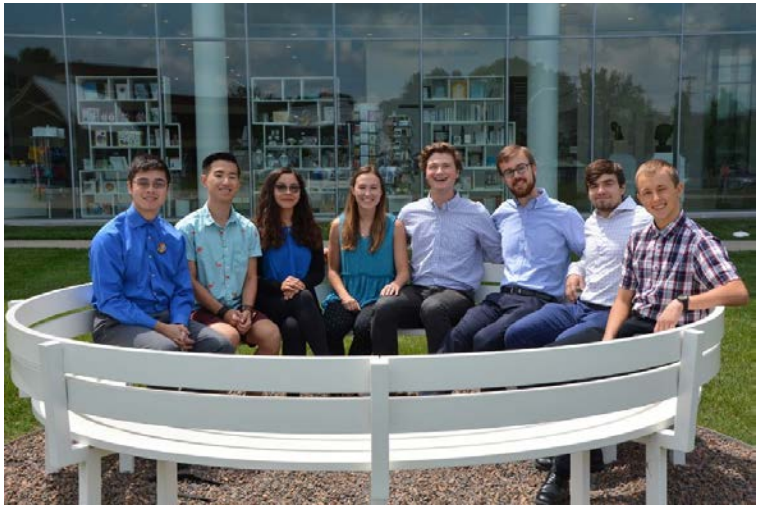
  Number: 1560235



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