Designing a Biodegradable Thin Film Drug Delivery Method for Use in Osteomyelitis Treatment

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Introduction

Osteomyelitis (Infection of the bone) poses a large risk for those who cannot get immediate access to strong antibiotics. Even when immediate medical access is available the standard solution is to Insert drug loaded PMMA beads using surgery (seen below). These beads must be removed at a later day resulting in 30% recurrence of osteomyelitis after 12 months.

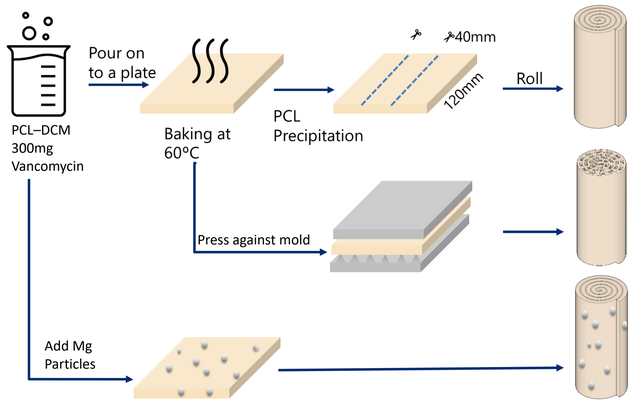
Figure 1:Going from left to right the first image depicts osteomyelitis and where it occurs, the second image depict doctors preparing drug eluting beads, the third images show an Xray of drug eluting PMMA beads implanted surgically.

Objectives

1. Make a solution that is **biodegradable**
2. Use **micro-channels** to control elution rate
3. Use **Mg micro-particles** to tune rate of elution

Materials and Methods

Using easily accessible Polycaprolactone (PCL) and vancomycin HCL from Sigma-Aldrich, the two can be combined using precipitation casting to form thin films. Phosphate buffered saline (PBS) is then used as the simulated human body fluid in which the rolls elute.



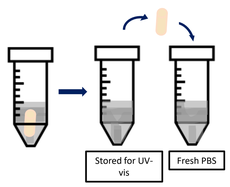


Figure 2: Illustration Depicting the process of forming the different through precipitation casting and adding the extra steps of pressing and adding magnesium for the 2 separates studies, respectively. The illustration directly to the right depicts the process of testing conducted to determine elution, in which the samples is moved to a fresh tube of PBS after a pre-determined amount of time in the previous tube.

Results

Morphology

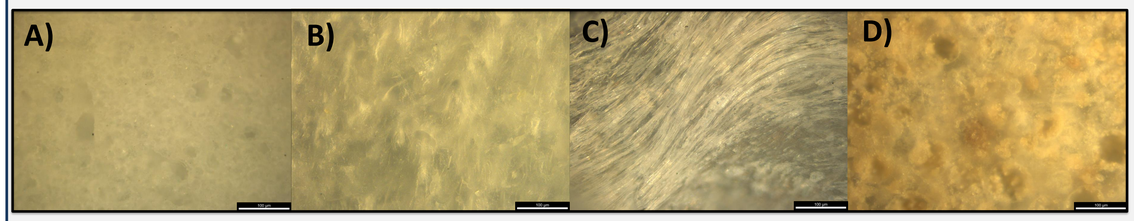


Figure 3: These are optical microscope taken at 20x in darkfield of the A) EDM Pressed, B) Ridged Pressed, C) Diffraction Pressed and D) 0.2% Mg Pre-elution.

Pressing samples against different surface **did not result in copying of the cast surface** onto the PCL but rather trapped solvent was able to use the channels in the ridged and diffraction surfaces to escape and flow out. This resulted in a morphological change in the samples as see in figure 3. This is seemingly attributable to changes in porosity and/or crystallinity of the PCL matrix.

Elution

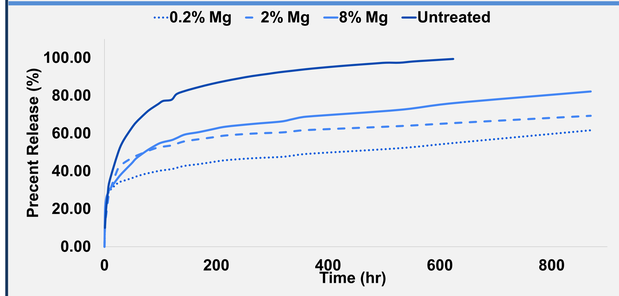


Figure 4: Cumulative release of vancomycin from PCL with various morphologies

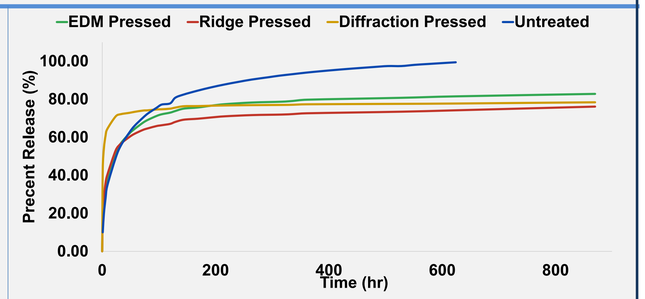


Figure 5: Cumulative release of vancomycin form Mg Enhanced PCL

From the results, the change in morphology causes a significant decrease in the elution. The trend is not obvious in the cumulative release, but it is apparent from the elution rate that the **more crystalline/less porous** the sample the **slower the elution.** Furthermore, **Introducing Mg** will **slow down the elution** at first, but further additions will begin increasing it.

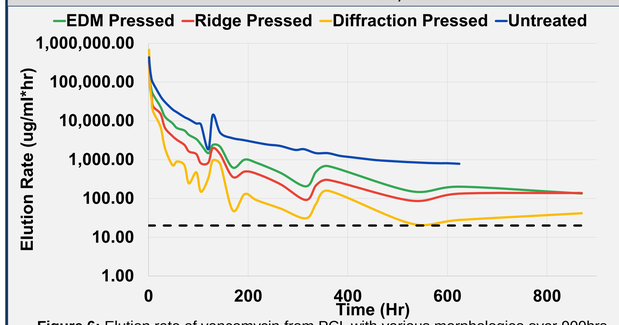


Figure 6: Elution rate of vancomycin from PCL with various morphologies over 900hrs

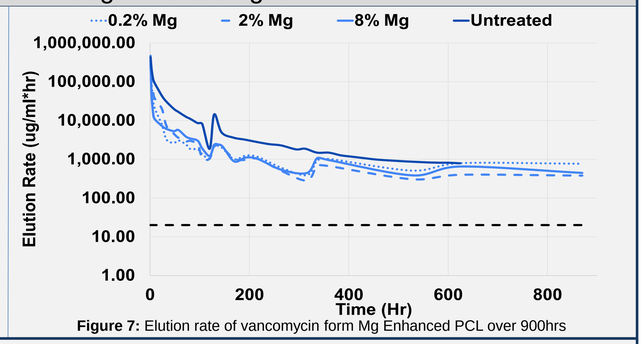


Figure 7: Elution rate of vancomycin form Mg Enhanced PCL over 900hrs

Analysis and Post Examination

Conducting differential scanning calorimetry on the pressed samples did not reveal a change in the crystallinity peak of PCL but there was a statistically significant difference between the melting temperatures of primary and secondary melts of the samples which means there is a morphological difference caused by the pressing process. This difference is irrecoverably destroyed once the samples are allowed to melt, resulting in all samples having similar melting temperatures during the secondary scan as seen in figure 8.

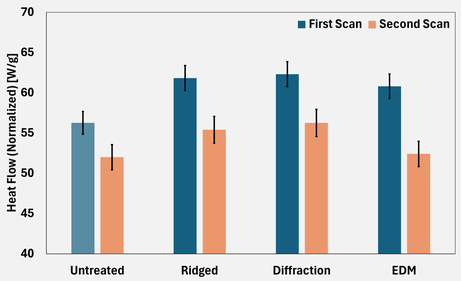


Figure 8: This Figure Show the melting temperature of the different samples during the primary and secondary scan with a heating rate of 5°C/min.

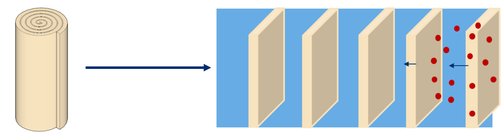
Conclusion

The release of vancomycin from PCL can be control by pressing against different surfaces to control morphology, although the specific morphological difference was not conclusively determined. Furthermore, using Mg microparticles in the PCL matrix will at first slow elution by increasing the surface area of the sample using bubbles and increasing the diffusion distance, but increasing concentration of Mg further triggers base catalyzed degradation of the PCL which seems to increase the elution of vancomycin. Using this two mechanisms it should be possible to create customized processing of PCL for specific elution profiles.

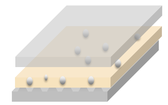
Future Work

This project has opened several key question that need to be address in future work as well as new potential combination of techniques that could be combine including:

1. Study the effect of smaller ranges of Mg microparticles.
2. Study the effect of large concentrations of Mg on inter layer pH and degradation.
3. Create models and from the data generated to determine the diffusion kinetics of vancomycin through the polymer.



1. Combine the two techniques and see how the morphology will interact with the Mg particles potentially leading to even slower elations.



Acknowledgements

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