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Controlled Release of Proteins with Hydralese® Formulations For Long-Acting Implants

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PURPOSE

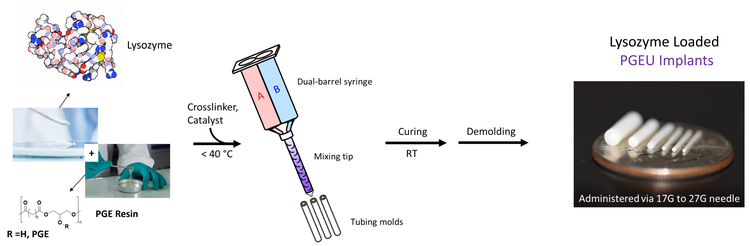
Controlled release of protein therapeutics offers unique advantages, such as reduced frequency of drug administration. However, developing systems that ensure controlled release while maintaining stability and intended activity remains a considerable challenge. Secant Group's Hydralese® drug delivery platform comprises a library of polyglycerolester urethanes (PGEUs) for controlled release of active pharmaceuticals (APIs) and biopharmaceutical ingredients. The drug release and polymer degradation profiles can be tuned by controlling the physicochemical characteristics of the polymer[1-4].

OBJECTIVES

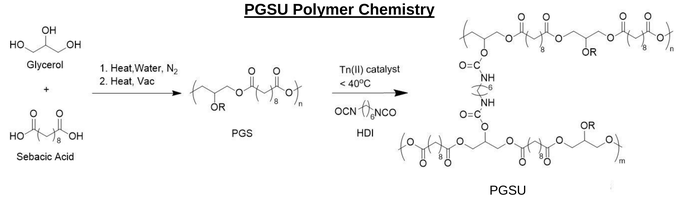
1. To manufacture Lysozyme loaded PGEU implants and develop methods for total drug assay content
2. To compare in vitro release profiles of Lysozyme from various PGEU formulations

METHODS

Two Part Implant Manufacturing Process Under Ambient Conditions



PGSU Polymer Chemistry



RESULTS

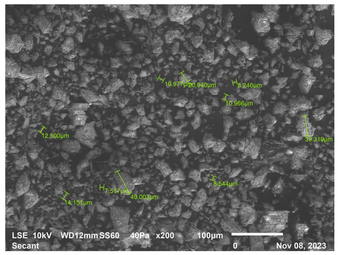


Figure 1: SEM image of tube-milled Lysozyme; particle size ranged from 5-100 µm

Figure 2: In-process Part A/Part B formulations pre-cure at 40% Lysozyme loading.

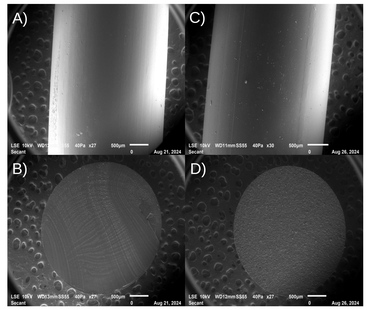


Figure 3: Lateral and Cross-sectional SEM images of unloaded (A-B) and 40% Lysozyme-loaded PGEUs (C-D) .

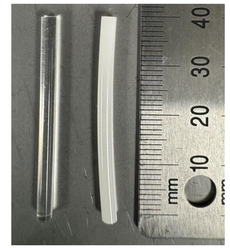


Figure 4: Images of unloaded (transparent) vs 40% Lysozyme loaded PGEU formulations.

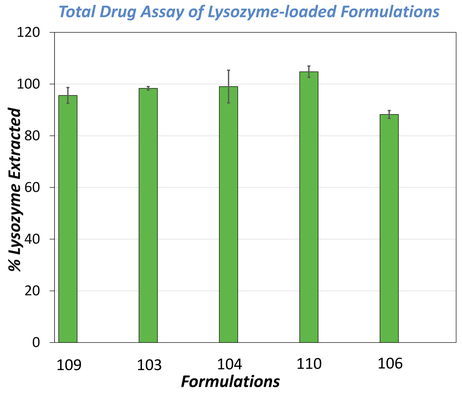


Figure 5: Total drug assay quantification of Lysozyme from different PGEU formulations; extractions are performed for 24 hours.

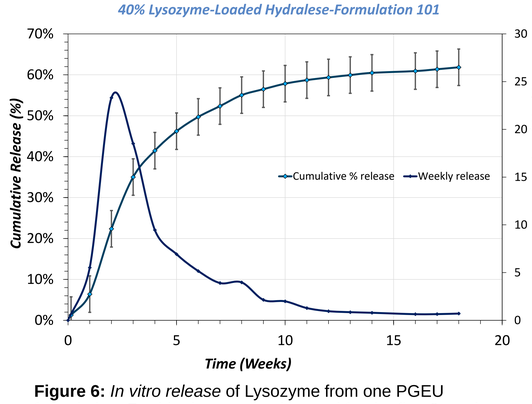


Figure 6: *In vitro release* of Lysozyme from one PGEU formulation; Rapid release was observed for the first 8 weeks and a cumulative release of 60% was observed at the end of 18 weeks.

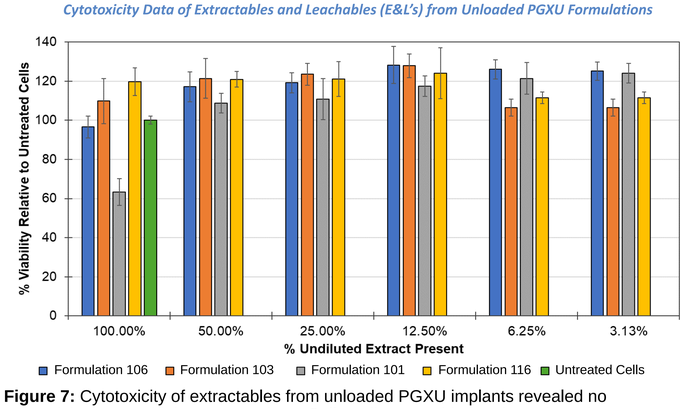


Figure 7: Cytotoxicity of extractables from unloaded PGXU implants revealed no cytotoxicity even at high concentrations. Cell media was added to the rods and extractions were carried out for 72 hours. Extracted media was then treated on fibroblast cells for 24 hours and XTT assay was performed to determine the cytotoxicity.

CONCLUSIONS

Successfully developed Lysozyme-loaded PGEU implants

- SEM images revealed ***no defects*** within the formulations
- Developed methods to ***rapidly*** quantify API content within loaded formulations
  - ***100% extraction*** from various formulations
- Long term release studies ongoing with various formulations
  - Sustained release observed until 18 weeks for formulation 101
- ***No cytotoxicity*** observed from extractables as measured by XTT assay
- Future studies include moderating initial burst release and developing methods to quantify activity of release lysozyme from IVR studies

REFERENCES

1. Nicholson, B. et al. US Patent 9,359,472, ***2016.***
2. Reed, S. et al. US Patent 10,918,764, ***2018.***
3. Reed, S. et. al. US Patent 11,406,732, ***2021.***
4. Reed, S. et. al. US Patent 11,883,557, ***2024.***

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