A Tunable, Biodegradable Drug Delivery with Hydralese® for Long-Acting Implants

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PURPOSE

The development of biodegradable polyurethanes for biomedical applications has garnered significant attention due to their potential benefits over non-degradable polyurethanes and conventional bioresorbable polyesters. Existing biodegradable polyesters such as poly(lactic-co-glycolic) acid (PLGA) and polylactic acid (PLA) lack the elastomeric properties needed to match the compliant viscoelastic behavior of native tissues, limiting their clinical applications and usability.

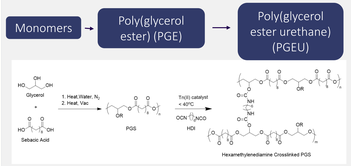
Secant Group's Hydralese® platform is a versatile polymeric delivery system that demonstrates tunable drug release and biodegradation rates for applications such as drug delivery, tissue engineering, and medical devices. Hydralese has a library of polymers based on poly (glycerol ester urethanes) (PGEU). In this study, cylindrical implants were formulated by loading a model API compound, 2'-deoxyadenosine (2'-dA), within Hydralese (PGEU)-based structures.

OBJECTIVES

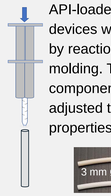
Our aim was to investigate the potential for: (a) PGEUs to provide sustained delivery of a small, hydrophilic drug, 2'-deoxyadenosine, based on the polymer cross-linking density, monomer composition, and molecular weights at high loadings for up to six months, and (b) tunable polymer degradation profiles.

METHODS

Implant Formulation



Formulation = Pre-polymer resin + 2'-dA + Diisocyanate crosslinker + Tin catalyst



API-loaded Hydralese devices were formulated by reaction injection molding. The ratio of components can be adjusted to tune device properties.

In Vitro Release and Polymer Degradation Conditions

- Release of the model API 2'-deoxyadenosine from PGSU rods into 10 mM PBS pH 7.4 at 3x sink conditions and 37°C and 50 RPM
- Media was monitored by HPLC with VWD.
- N=9 rods were chosen per formulation.
- N=2 samples were pulled at each timepoint for SEM characterization, mass analysis and API extraction.
- Extractions were performed in DMSO on samples pulled at 3 months and 6 months to confirm the amount of 2'-dA remaining in the sample.

RESULTS

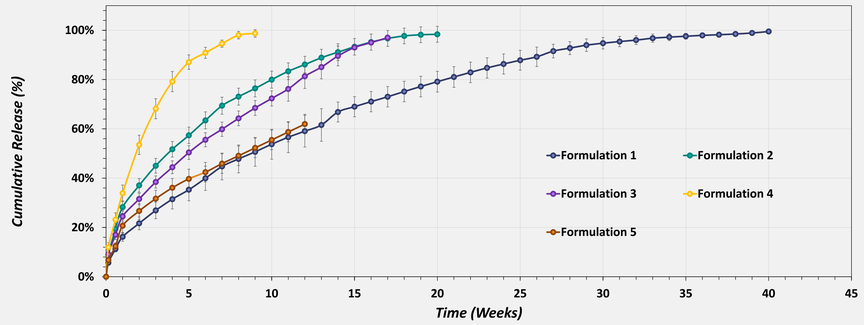


Figure 1. *In vitro* release kinetics of 40% (w/w) 2'-dA-loaded PGEU cylindrical rods (3 mm Ø x 40 mm L)

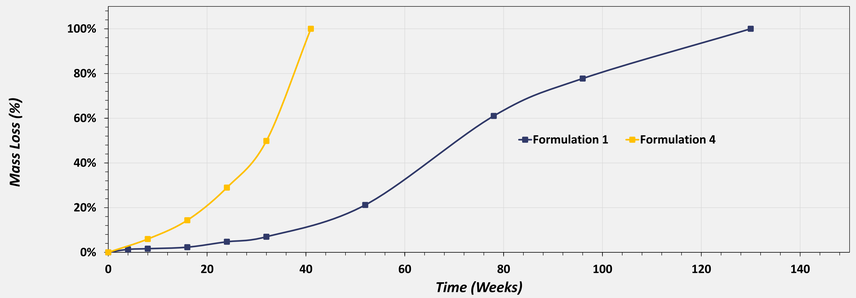


Figure 3. *In vitro* polymer degradation profiles for unloaded PGEU from Formulation 1 and 4

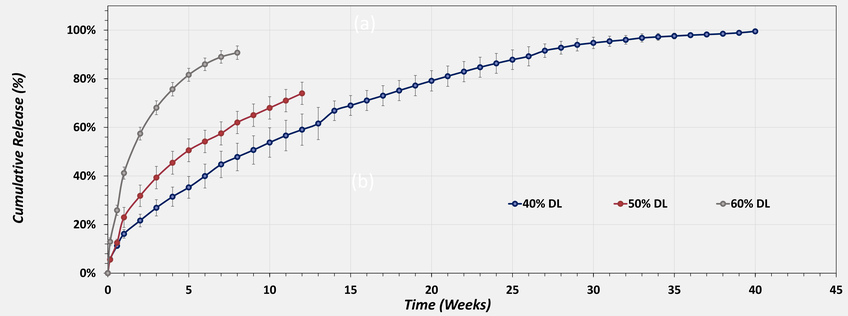


Figure 2. *In vitro* release kinetics of 40 weeks for 40%, 50% and 60% (w/w) 2'-dA-loaded Formulation 1 composition cylindrical rods (3 mm Ø x 40 mm L); 2'-dA release for 50% and 60% (w/w) formulations are still ongoing.

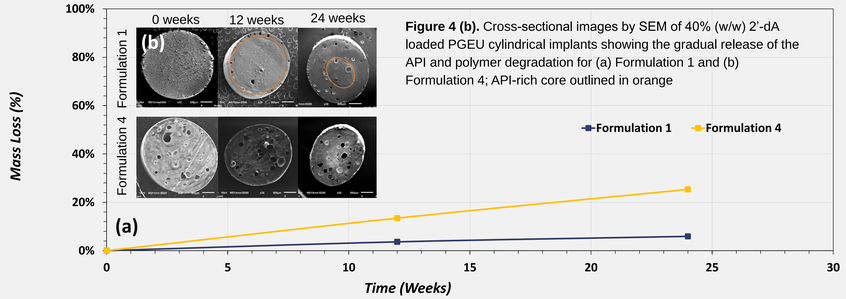


Figure 4 (b). Cross-sectional images by SEM of 40% (w/w) 2'-dA loaded PGEU cylindrical implants showing the gradual release of the API and polymer degradation for (a) Formulation 1 and (b) Formulation 4; API-rich core outlined in orange

Figure 4 (a). *In vitro* polymer degradation profiles for 40% (w/w) 2'-dA-loaded PGEU cylindrical rods per Formulation 1 and 4 up to 6 months of *in vitro* release

CONCLUSIONS

- 2'-deoxyadenosine was successfully loaded into flexible, solvent-free PGEU implants at 40%, 50% and 60% (w/w) loadings under ambient conditions
- API release kinetics show devices can be tuned to release drug payloads from 10 weeks up to 40 weeks for small, hydrophilic drugs
- Higher drug loadings and use of more hydrophilic pre-polymer resins result in faster release profiles
- Hydralese provides a library of polymers with *in vitro* degradation profiles from 3-12+ months

PGEU implants are an attractive carrier providing efficient pharmokinetics and long-acting treatment at higher loadings for small, highly water-soluble drugs, such as 2'-dA.

REFERENCES

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