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Hydralese®: A tunable polymer platform for long-acting drug delivery

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secant.com/drug-delivery

Innovating novel solutions

Advancing small and large molecule delivery

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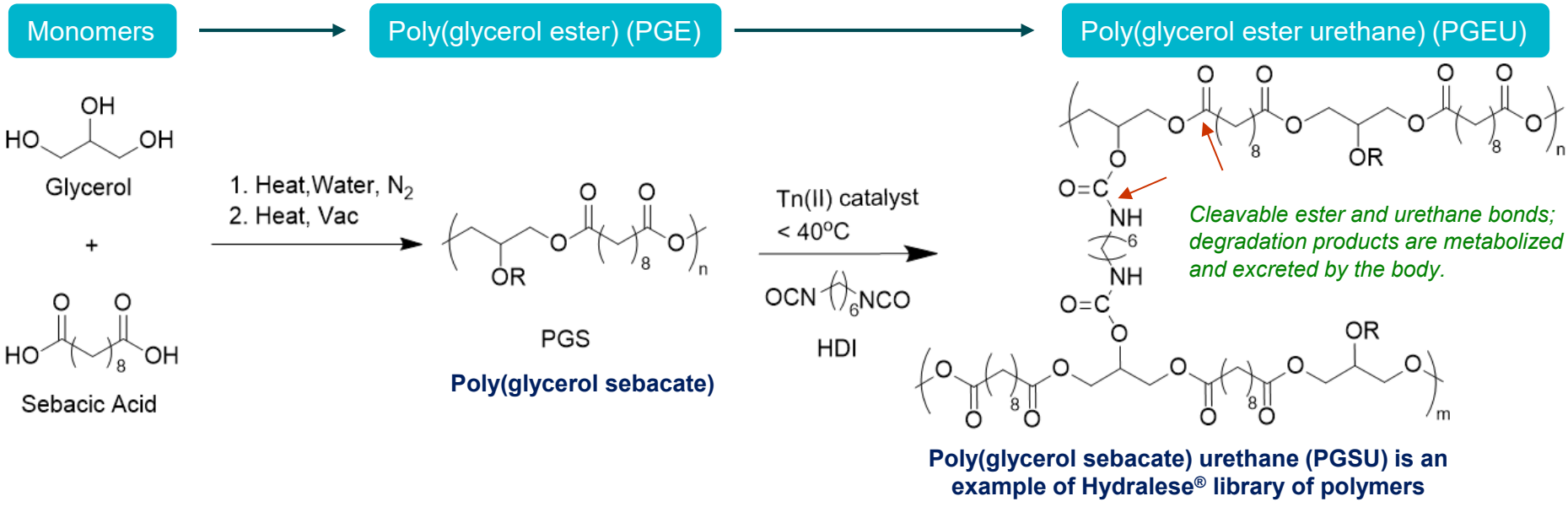
Drug delivery with Hydralese® library of biodegradable polymers for tunable controlled release of small and large molecule APIs

Poly(glycerol ester) (PGE)

Ready-to-use nanoparticles for nucleic acid therapeutics delivery

Drug Delivery with Hydralese

Polymers for controlled release of active pharmaceuticals and biopharmaceutical ingredients



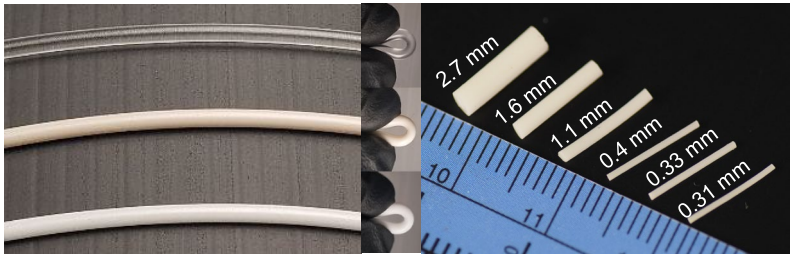
Poly(glycerol sebacate) urethane (PGSU) is an example of Hydralese® library of polymers

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

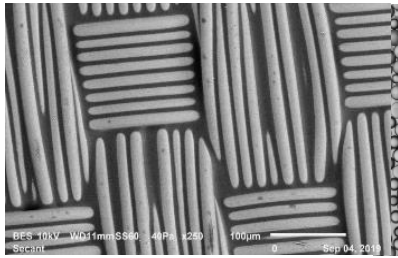
Form Factor Options with Hydralese

Versatility for multiple routes of administration

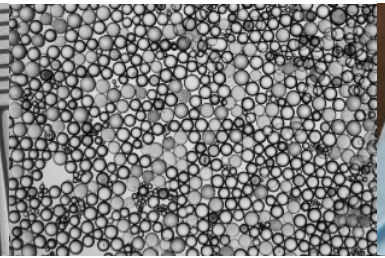
Solid Implants of Various Diameters & Core/Sheath Implants



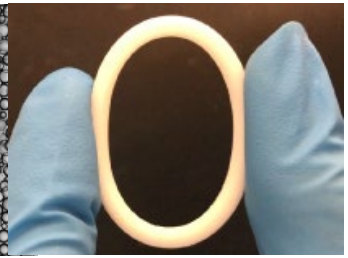
Coatings



Injectable Microparticles



Closed Geometry



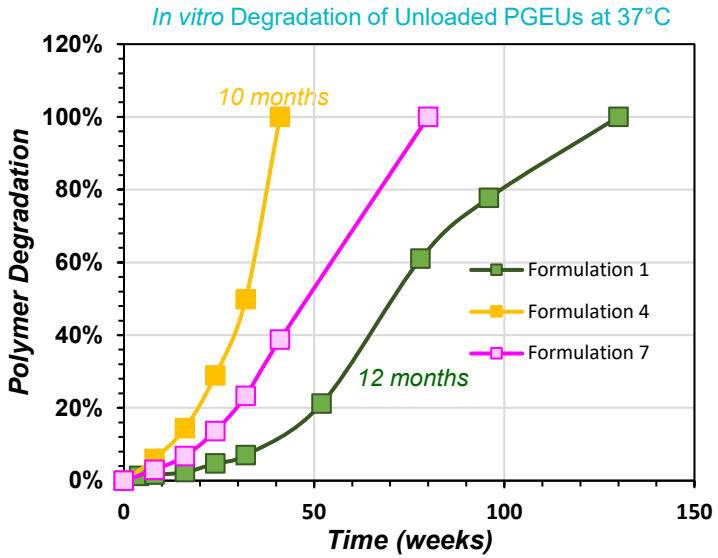
Attributes	PGSU Specifications
Tensile Modulus	10-12 MPa
Flexural Modulus	9-12 MPa
Biocompatibility	USP Class VI and ISO 10993 testing showed no adverse reactions
Degradation Timeframe	3 to 12+ months
Crosslinking	Ambient conditions
Manufacturing Processes Compatible with PGSU	Extruding, molding, casting, coating, emulsification
Storage	Room temperature and humidity for 6 months
Sterilization	Stable at 18-29 kGy and 25-34 kGy gamma irradiation
Type IV DMF for PGSU (will continue to expand)	On file with FDA for PGSU

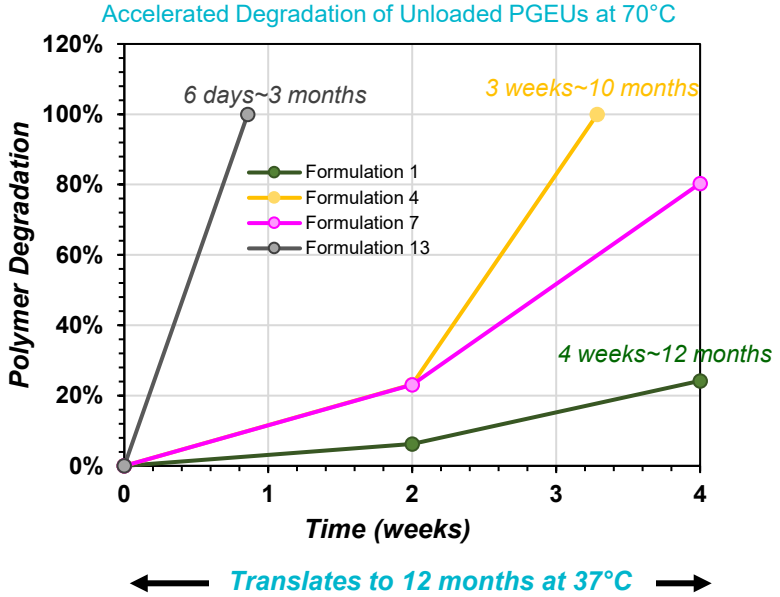
Tunable degradation behavior of Hydralese polymer library

Modifying monomers, molecular weight, hydrophobicity/hydrophilicity, and crosslinkers

Unloaded Implant Study

- Unloaded PGEUs were placed in 6-15 mL of 0.1 M PBS at 37°C or 70°C
- Samples were placed on an orbital shaker at 230 RPM



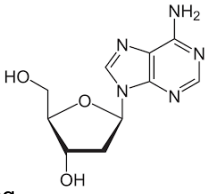


Tunable *in vitro* release

With water-soluble 2'-deoxyadenosine

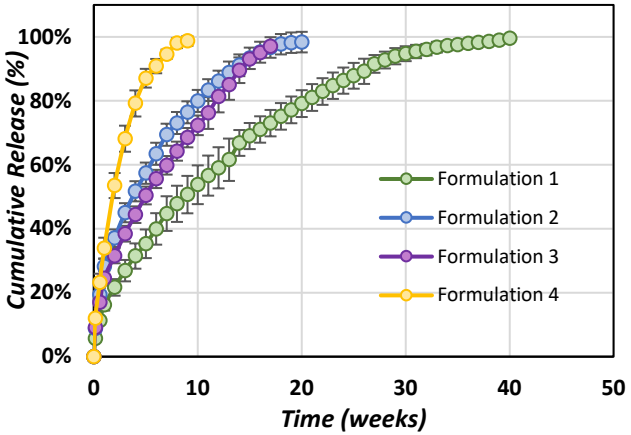
Small Molecule Study

- 2'-deoxyadenosine is a deoxyribonucleoside with a molecular weight of 251.2 g/mol
- Its solubility in 10 mM PBS is 3.5 mg/mL
- D_{50} of 2'-deoxyadenosine used in these formulations is 4.3 µm
- Implants were 3 mm in diameter and 40 mm in length
- *In vitro* release was carried out in 10 mM PBS at 6x sink conditions and 50 rpm orbital shaking
- Dissolution media was replaced at every timepoint
- Total drug assay showed 100% drug encapsulation

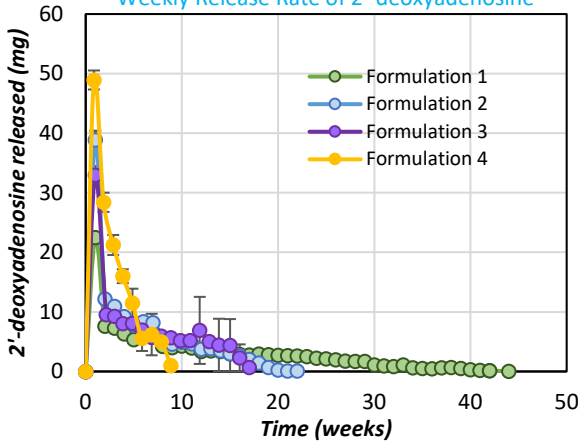


Tunable release between 10 & 40 weeks depending on formulation type

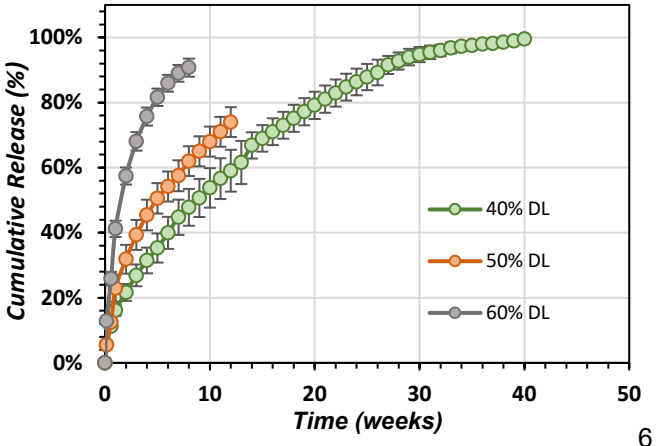
Cumulative release from 40% loaded formulations



Weekly Release Rate of 2'-deoxyadenosine

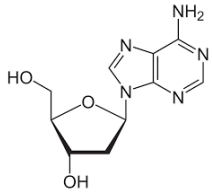


Formulation 1: Effect of % Drug Loading



Comparing PLGA and PCL to Hydralese

Hydralese shows linear release of water-soluble 2'-deoxyadenosine *in vitro*

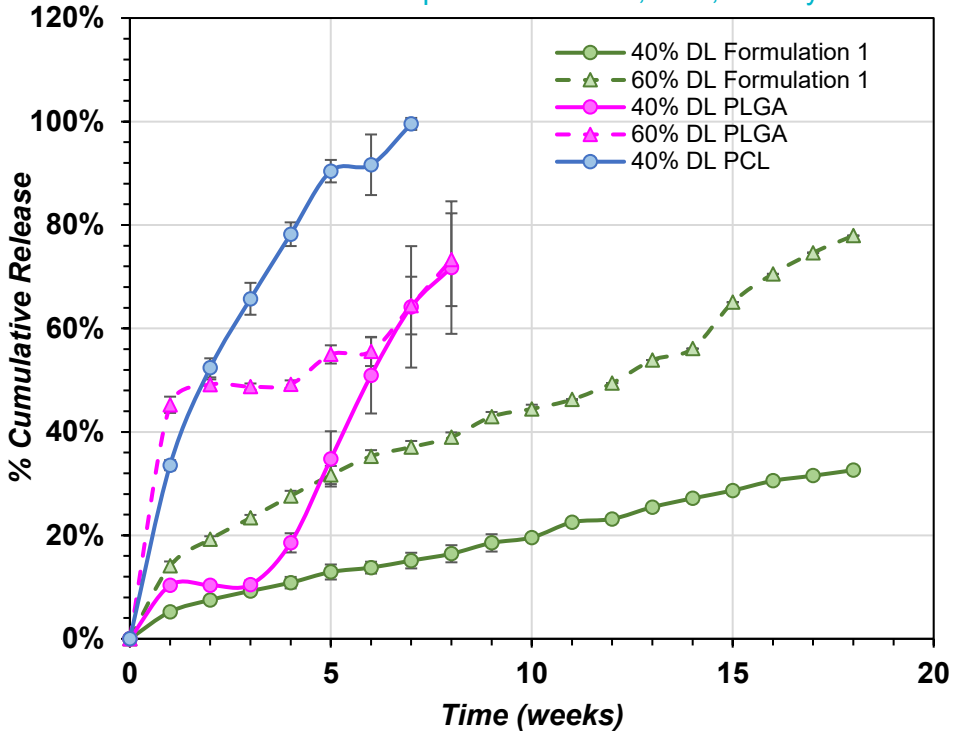


Small Molecule Comparison Study

- 2'-deoxyadenosine is a deoxyribonucleoside with a molecular weight of 251.2 g/mol
- Its solubility in 0.1 M PBS is 3.5 mg/mL
- Implants are 3 mm in diameter and 40 mm in length
- *In vitro* release was carried out in 0.1 M PBS in Dissolution App IV at 5x sink conditions
- Aliquots were taken an each timepoint and replaced

Hydralese shows zero order kinetics as compared to PLGA and PCL

In vitro Release Comparison of PLGA, PCL, and Hydralese



Total Drug Assay of Lysozyme from Hydralese

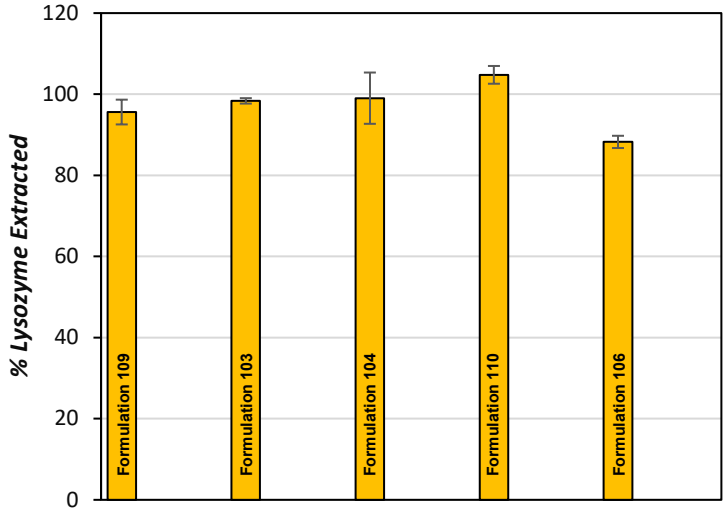
100% drug extraction

Large Molecule Study

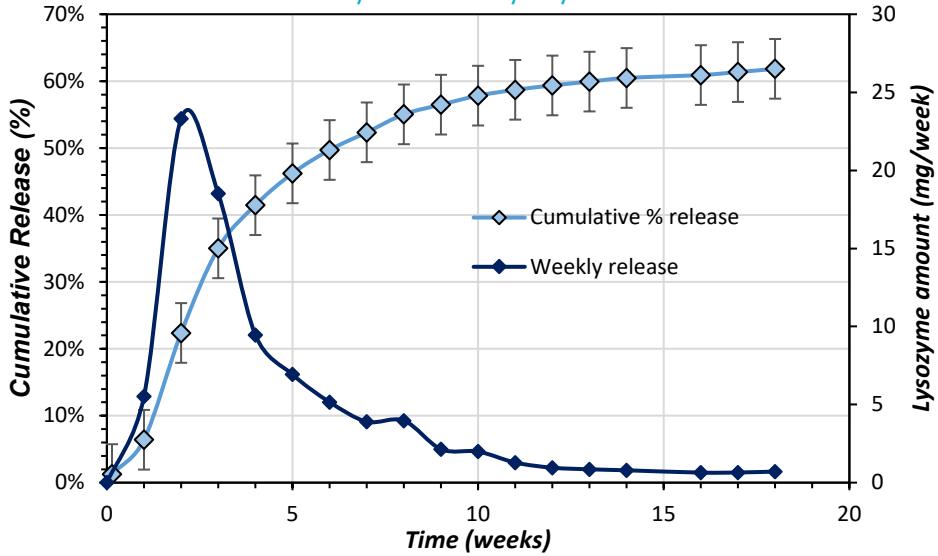
- Lysozyme is a protein with a compact, globular structure containing 129 amino acids and a molecular weight of 14.3 kg/mol
- Its solubility in 10 mM PBS is 100 mg/mL
- Lysozyme used in formulations was tube milled to 5-100 µm
- *In vitro* release was carried out in 10 mM PBS at 5x sink conditions and 50 rpm orbital shaking
- Total drug assay was performed by extracting native lysozyme in 24 hours

100% Lysozyme was extracted in 24 hours

Total drug assay of Lysozyme-loaded Formulations

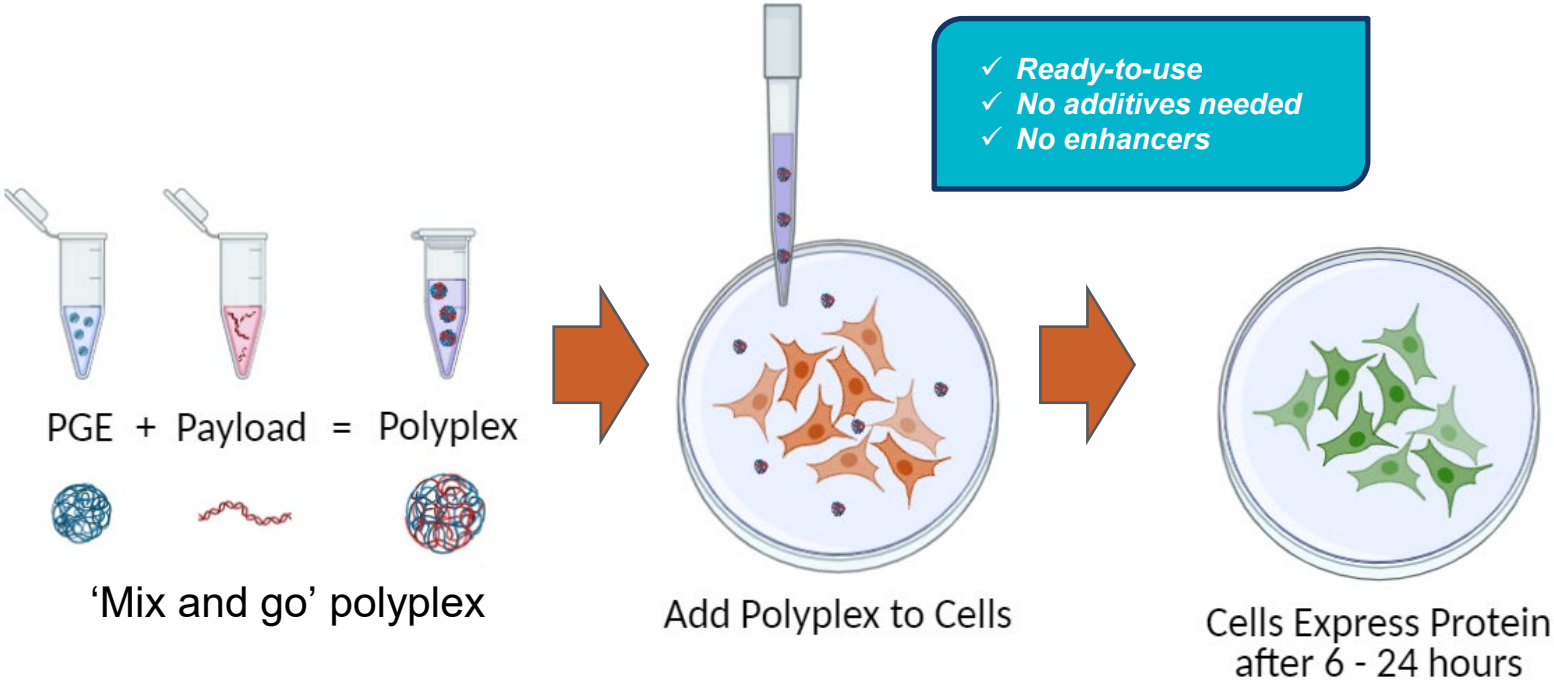


Cumulative and Weekly Release of Lysozyme from Formulation 101



Delivering Nucleic Acids to Cells with Poly(glycerol esters)

Nanoparticle polyplex form

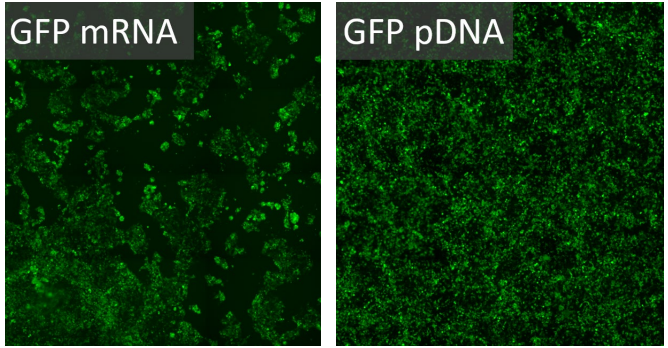


Deliver mRNA and pDNA to Transfect Cells

With PGE polyplex nanoparticles

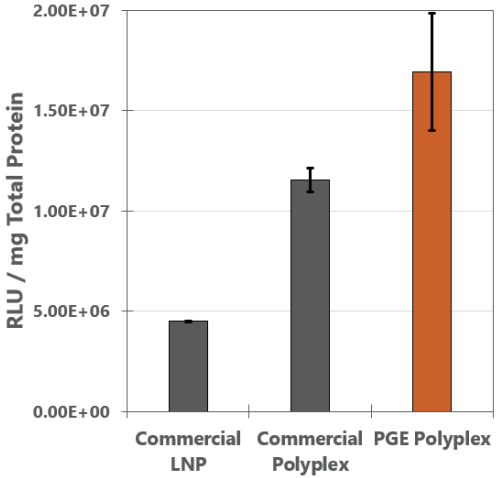
PGE can deliver mRNA and pDNA

A high percentage of HEK293T cells express GFP reporter protein after 24 hours when transfected with plasmid DNA or messenger RNA.



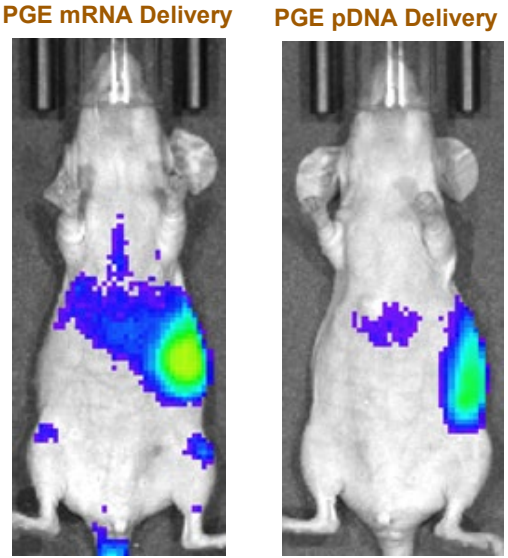
PGE improves protein yield

Delivery of luciferase pDNA to HEK293T cells using PGE polyplex yields superior protein production after 24 hours compared to commercial reagents.



PGE can deliver mRNA and pDNA *in vivo*

PGE nanoparticles are able to deliver nucleic acids *in vivo* with expression seen within the first six hours following tail vein injection for delivery (below).



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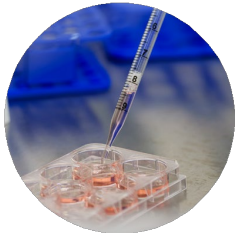
Drug Delivery with Hydralese

Library of polymers for controlled release

- ✓ 3 to 12+ months sustained delivery of small molecule APIs and biologics
- ✓ Tunable for optimal release kinetics and degradation profiles
- ✓ Versatile poly(glycerol ester urethane) (PGEU) synthesized into multiple form factors



Nucleic Acid Therapeutics Delivery

***In vitro* and in vivo delivery with poly(glycerol ester) (PGE) nanoparticles**

- ✓ Ready-to-use with no additives and no enhancers needed
- ✓ Delivers nucleic acid therapeutics, such as mRNA and pDNA

Partner with Secant Group

Develop your next-generation delivery innovation

- ✓ Decades of polymer expertise
- ✓ Proprietary, patent-protected and biodegradable polymer platforms
- ✓ ISO-17025:2017-accredited analytical testing lab
- ✓ ISO-certified Class 7 & 8 cleanrooms

Contact: Manasi Baker
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