Next Generation Long-acting Implantables Using Surface-eroding Elastomers

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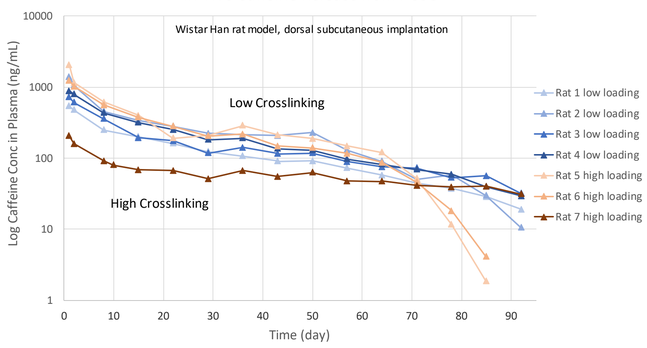
secant group
PARTNERS FROM INSPIRATION TO REALIZATION

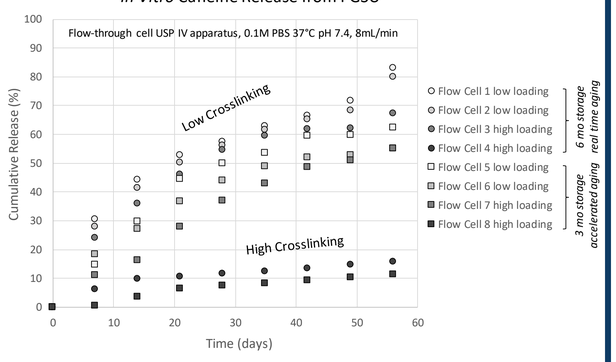
Hydralese™ (PGSU) (poly(glycerol sebacate) urethane) (Secant Group) is a synthetic biodegradable elastomer for controlled drug release. Hydralese (PGSU) is elastomeric, water impermeable, shelf-life stable, biocompatible, and biodegradable via surface erosion. Unlike bulk-eroding polymers or non-degradable polymers that rely on diffusion, Hydralese's (PGSU) hydrolytic surface erosion confers near zero-order release kinetics, even at high drug loadings, and maintains a near-constant release rate across drug loadings. Hydralese (PGSU) can be loaded with both hydrophilic and hydrophobic drugs up to 80% w/w. The active pharmaceutical ingredient (API) is incorporated by blending the neat powder with PGS polyol resin prior to urethane reaction. Solvent extraction methods demonstrate no observable cross-reaction of API into the polymer network during urethane crosslinking, nor are any detrimental or cross-reaction effects observed after gamma sterilization. The two-component Hydralese (PGSU) reaction demands thorough mixing within its pot life to achieve API content uniformity and crosslinking uniformity. Hydralese's (PGSU) crosslinking density is critical to reducing fluid percolation in and API permeation out of the matrix, especially at high drug loadings, thereby limiting burst release and diffusion, so that the delivery is truly driven by surface erosion. Hydralese (PGSU) is an attractive delivery system for very hydrophobic drugs, which otherwise may not be able to diffuse out of the matrix, and for very hydrophilic drugs, which otherwise may have an uncontrolled burst release. Ultimately, Hydralese (PGSU) offers many advantages over other polymers for long-acting implantables (LAIs), particularly for high-loading, long-duration implants that are gaining interest in the pharmaceutical industry.

Hydralese (PGSU) Crosslinking Predicts Near Zero-order Release Rate

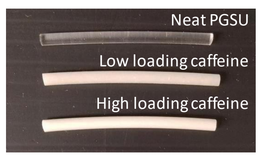
In Vivo Caffeine Release from PGSU



In Vitro Caffeine Release from PGSU

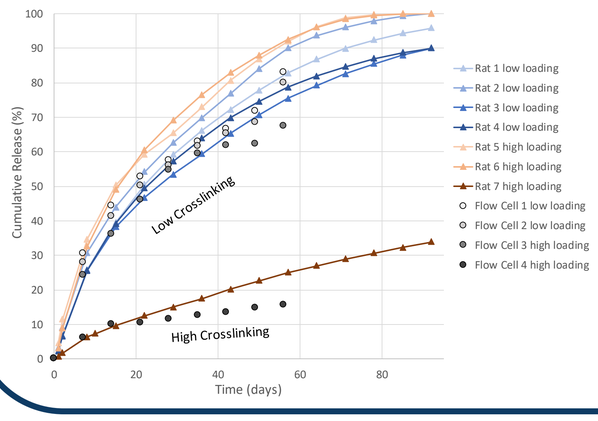


Implant	Crosslinking Density (mol/L)	Initial Loading (%)	Residual Loading (%)
Rat 1	0.85	20.9	0.7
Rat 2	0.86	18.2	0.0
Rat 3	0.89	18.3	N/A
Rat 4	0.51	19.6	N/A
Rat 5	0.65	24.8	0.0
Rat 6	0.64	25.3	0.0
Rat 7	2.75	23.7	18.9

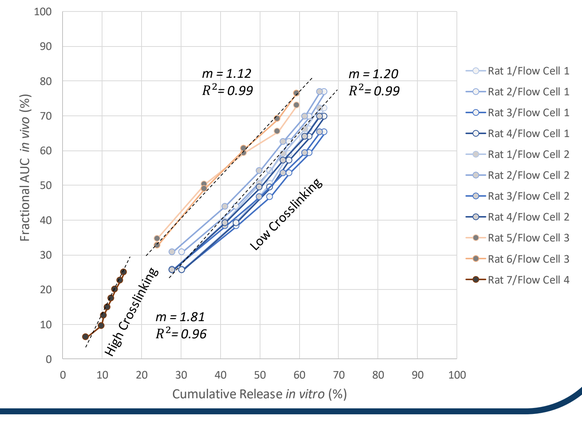


Implant	Shelf Life Storage Condition	Initial Loading (%)
Flow Cell 1	6 mo real time aging	14.6
Flow Cell 2	6 mo real time aging	14.9
Flow Cell 3	6 mo real time aging	24.8
Flow Cell 4	6 mo real time aging	19.3
Flow Cell 5	3 mo accelerated aging	12.1
Flow Cell 6	3 mo accelerated aging	15.7
Flow Cell 7	3 mo accelerated aging	24.6
Flow Cell 8	3 mo accelerated aging	20.5

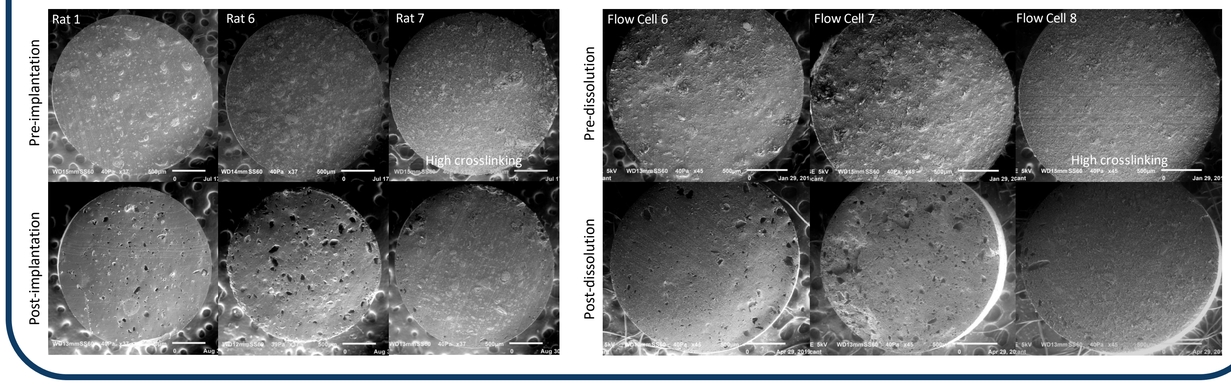
In Vivo - In Vitro Overlay



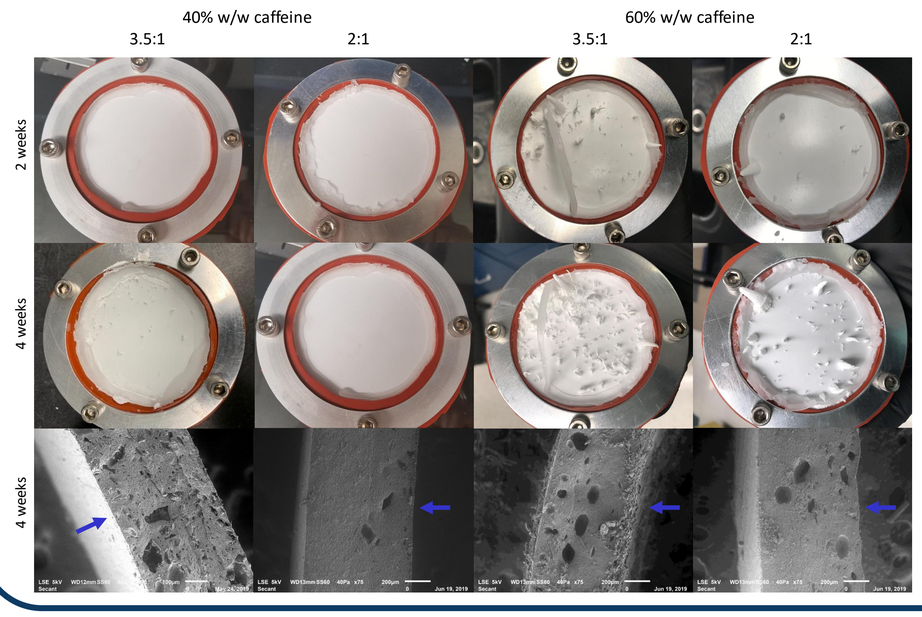
In Vivo - In Vitro Correlation



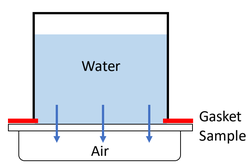
Hydralese (PGSU) Crosslinking Reduces Diffusion and Burst Release



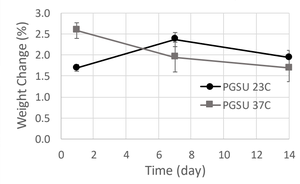
Hydralese (PGSU) Crosslinking Reduces Percolation and Permeation



Inverted Cup Method ASTM E96

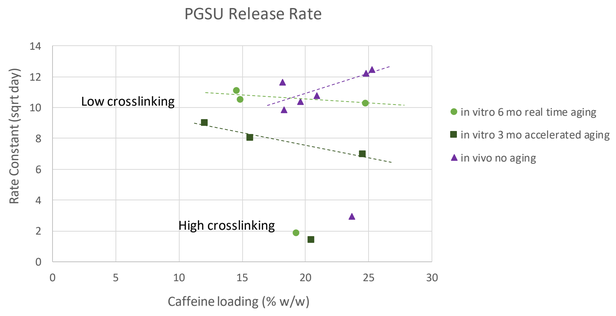


Neat PGSU Swellability

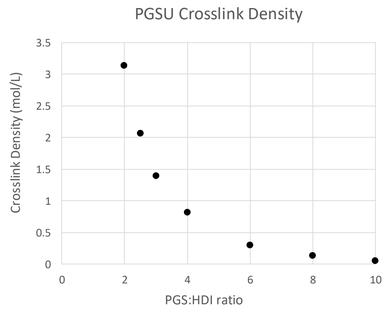


Hydralese (PGSU) Release Rate Is Near-constant Across Drug Loadings

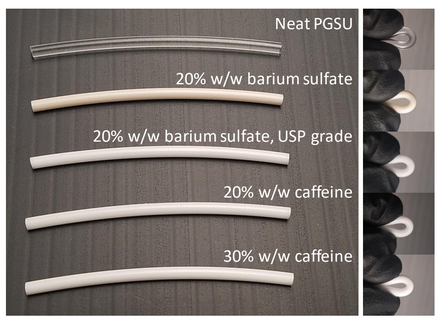
PGSU Release Rate

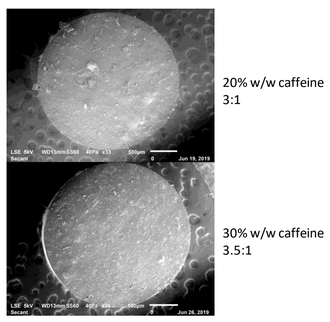


PGSU Crosslink Density

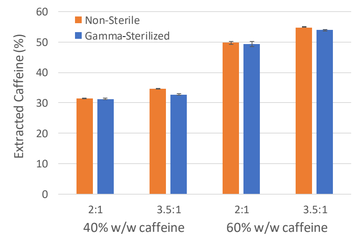


Hydralese (PGSU) Performs Reliably as an Elastomeric Matrix for LAIs

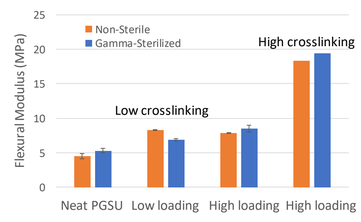




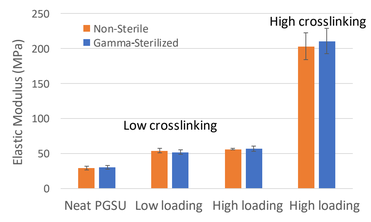
Solvent Extraction from PGSU



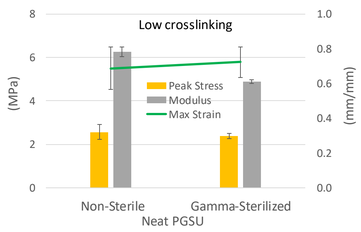
3 Point Bending of PGSU Implant

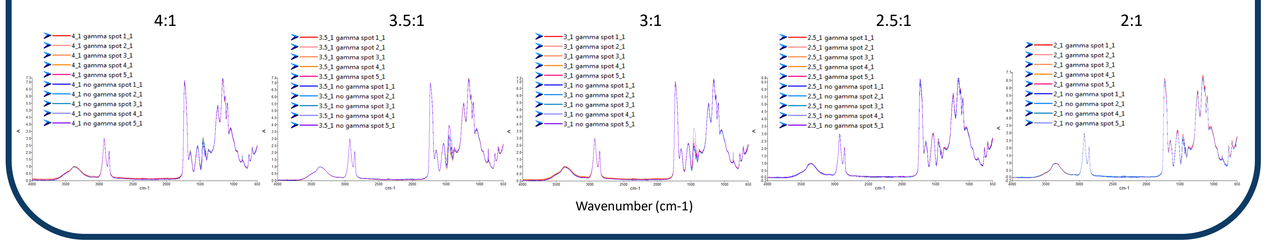


Axial Compression of PGSU Cross Section

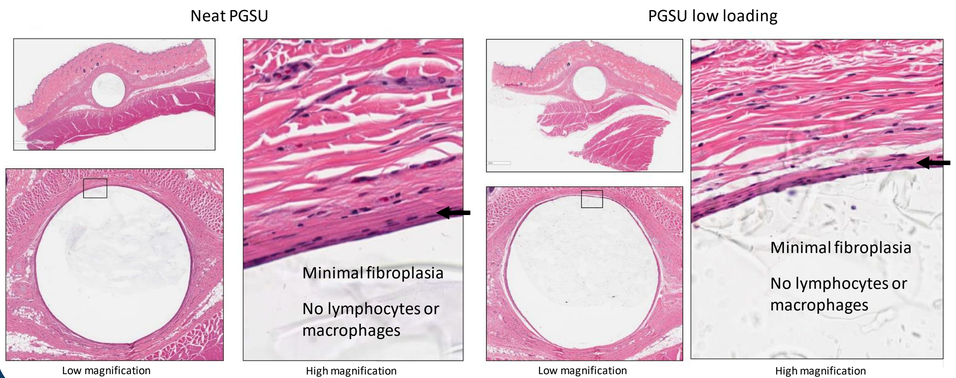


Axial Tension of PGSU Sheet





Hydralese (PGSU) Demonstrates Biocompatibility Without Fibrosis



ISO 10993 Test	Scoring
Cytotoxicity	0/0/0
Acute Systemic Toxicity	0/0/0/0/0
Irritation	0/0
Implantation	0/0