Ultra-long-acting Oral Drug Delivery Using a Single-component Hydralese™ (PGSU) Gastroretentive Device

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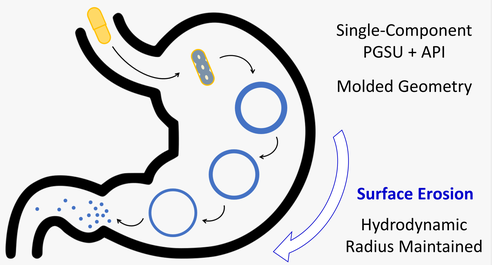
PURPOSE

Secant Group has developed a biodegradable, biocompatible elastomer for long-acting drug delivery called Hydralese™ (PGSU) (poly(glycerol sebacate) urethane). Secant Group has previously shown that Hydralese (PGSU) can achieve steady release of active pharmaceutical ingredients (APIs) for multiple weeks to even more than a year, based on the polymer crosslinking density and degradation rate. Hydralese (PGSU) maintains its mechanical form for longer periods of time without losing mechanical integrity because it hydrolytically surface erodes. It also maintains excellent flexibility and controlled release at up to 80% w/w drug loading. This elastic resilience, surface erosion degradation, and high API loading capacity, combined with steady release over long durations, make Hydralese (PGSU) an attractive option for ultra-long-acting oral delivery via a gastroretentive device. The confluence of these properties allows the entire gastroretentive device to be composed of a single component of drug-loaded Hydralese (PGSU).



Hydralese (PGSU) for Gastroretentive Devices

METHOD(S)

PGSU solvent-free: Poly(glycerol sebacate) (PGS) resin mixed with hexamethylene diisocyanate (HDI) at 3.5:1 w:w for nominal crosslinking and 2:1 w:w for high crosslinking

PGSU solvated: 60% w/w PGS resin in 1:1 w:w acetone:propyl acetate mixed with HDI at 3.5:1 w:w

PGSU caffeine-loaded: 40% w/w caffeine powder blended into PGS resin mixed with HDI at 3.5:1 w:w

Manufacturing: Dual-barrel syringe extrusion through a static mixing tip into molds shaped for rods and rings

Acidic Media: Simulated gastric fluid (SGF) at pH 1.22
Basic Media: Triethylamine (TEA) at pH 11.44

Simulated Gastroretention Conditions: 37°C, acidic media
Real Time Degradation Conditions: 37°C, acidic media
Forced Degradation Conditions: 70°C, acidic/basic media

RESULT(S)

Hydralese (PGSU) Device Flexibility

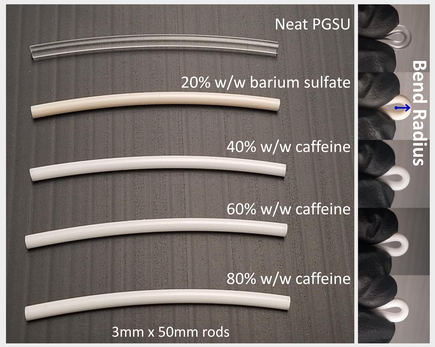


Figure 1: Hydralese (PGSU) rods, both neat and loaded with various model APIs, shown straight and folded in half to demonstrate flexibility and bend radius.

Hydralese (PGSU) Devices Loaded into and Released from Gelatin Capsules

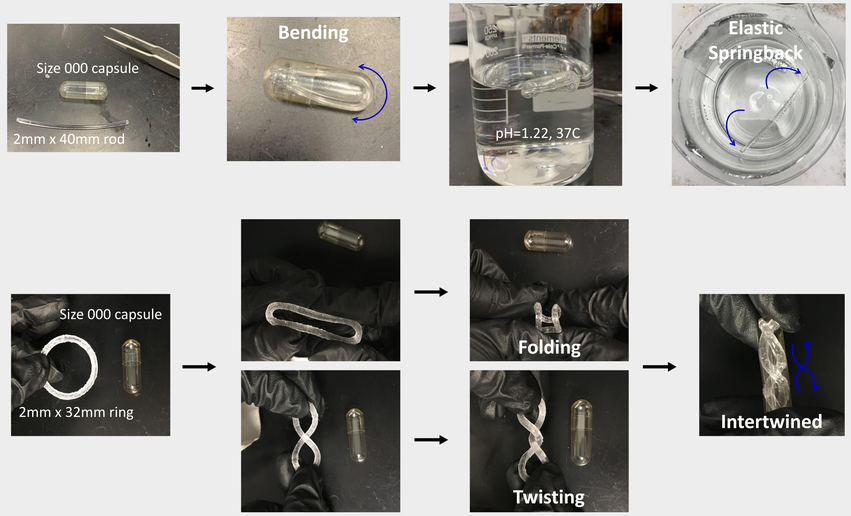


Figure 2: Hydralese (PGSU) gastroretentive devices, in rod and ring shapes, loaded into gelatin capsules through bending, folding, or twisting. Devices exhibited springback and elastic recovery after capsule disintegration in SGF.

Real-time Degradation of Caffeine-loaded Hydralese (PGSU), 37°C

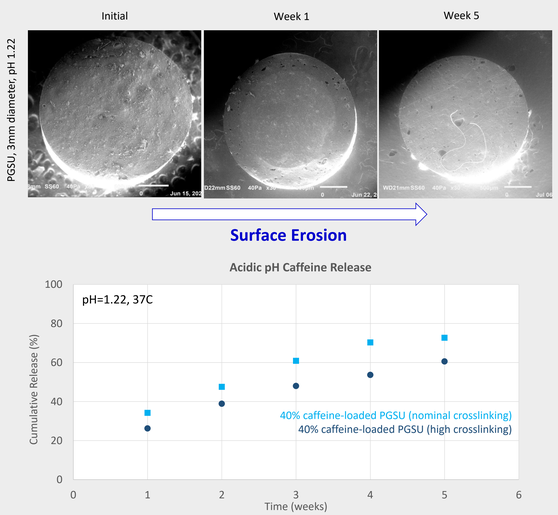


Figure 3: Nominal and high crosslinking Hydralese (PGSU) rods, made with a solvent-free formulation containing 40% w/w caffeine, subjected to degradation and dissolution in pH 1.22 SGF at 37°C.

Forced Degradation of Hydralese (PGSU), 70°C

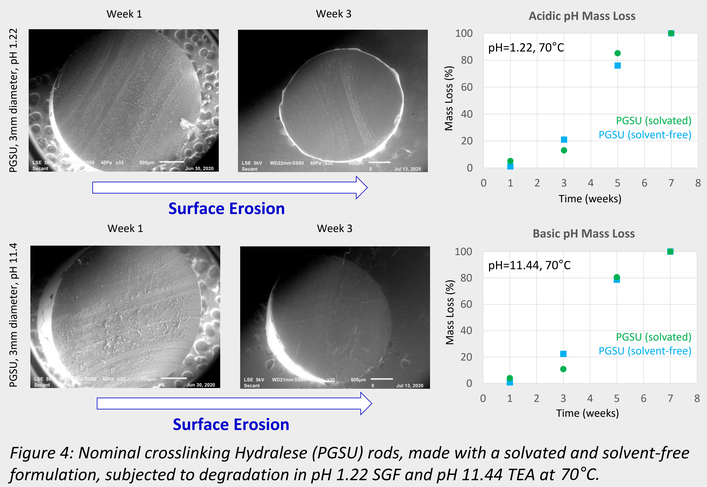


Figure 4: Nominal crosslinking Hydralese (PGSU) rods, made with a solvated and solvent-free formulation, subjected to degradation in pH 1.22 SGF and pH 11.44 TEA at 70°C.

CONCLUSION(S)

A drug-loaded Hydralese (PGSU) device can be cast or reaction injection molded into complex geometries as a single part, reducing time and cost over multi-component device manufacturing methods. Molded Hydralese (PGSU) devices, such as rings and rods, can be folded or twisted into gelatin capsules for oral intake yet spring back with full elastic recovery upon capsule disintegration. Since Hydralese (PGSU) surface erodes, the device maintains a large hydrodynamic radius throughout its degradation in the stomach, preventing it from passing through the pyloric sphincter prematurely. Hydralese (PGSU) also presents a safer and more comfortable option for gastroretentive drug delivery. Due to the flexibility of Hydralese (PGSU) throughout degradation and because Hydralese (PGSU) surface erodes into micro-scale fragments, there is less risk of blockage, puncture, and irritation within the stomach and bowel. Even in highly acidic and basic conditions relevant to the stomach and intestine, Hydralese (PGSU) sustains multi-month API delivery and surface erosion degradation behavior, fulfilling an unmet need for ultra-long-acting oral delivery.

Hydralese™ Biodegradable Elastomers

REFERENCES

1. Reed, S., inventor; Secant Group, assignee. Shape-guided controlled release and retention with structures including crosslinked poly(glycerol sebacate). US patent application 63/057,952. Filed July 30, 2020.
2. Reed, S., inventor; Secant Group, assignee. Tunable, controlled-release, urethane-containing elastomers and processes of forming the same. US patent application 16/547,175. Filed August 21, 2019.
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