Engineering a Retrievable "Bead-on-a-String" Polymeric Array for Localized Drug Delivery

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Introduction

The Problem: Post-surgical infections require immediate, high-dose, localized antibiotic treatment without the risk of device migration.

The Solution (Figure 1): An interconnected microparticle array ("bead-on-a-string") that anchors to the wound bed, conforms to tissue, and enables highly controlled release and monitoring.

Objective: Evaluate polymer matrices to identify a structurally stable formulation capable of sustained, high-capacity localized delivery of Rifampin at 37° C.

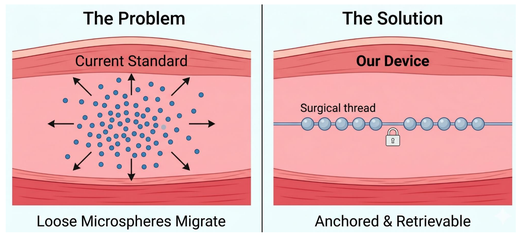

Figure 1: *Clinical deployment of the retrievable array in a C-section wound bed. The interconnected depots prevent migration, providing sustained localized analgesia with an instant mechanical retrieval failsafe.*

Methods

Standardized Depots: Custom V2 3D-printed open-face molds created identical 125 µL interconnected microparticle arrays spanning a central 0.5 mm thread trench.

Matrix Fabrication: Evaluated architectures included:

1. **Physical Hydrogels:** 10% (w/v) uncrosslinked Gelatin.
2. **Composite Barriers:** PLGA dip-coated Gelatin and freeze-thawed PVA cores.
3. **Structural Shells:** Solvent-cast, vacuum-evaporated hollow PLGA.
4. **Synthetic Networks:** PPODA-QT crosslinked via Michael addition (Pre-loaded vs. Solvent-swelled post-loading).

Release Protocol: In vitro Rifampin release testing in PBS at 37° C. A strict "**Complete Media Replacement**" methodology was utilized to maintain sink conditions. Release kinetics were evaluated by comparing the absolute cumulative mass (mg) of Rifampin delivered.

Figure 2: *Custom 3D-printed V2 casting molds (125 µL cavity) featuring a central trench to accommodate the surgical thread backbone.*

Results

Phase 1 & 2: Physical Instability & Barrier Failure

- Uncrosslinked 10% gelatin failed at 37° C, undergoing rapid macroscopic degradation within 2 hours.
- Attempting to bottleneck release via a PLGA dip-coating yielded failure modes: Gelatin cores absorbed PBS and physically fractured the PLGA shell.
- **(See Burst Phase Inset):** While PLGA-coated PVA and Hollow PLGA shells maintained structural integrity, they exhibited rapid dose-dumping, plateauing entirely within the first 2 hours of deployment.

Phase 3: Synthetic Stability & Sustained Delivery

- Transitioning to synthetic PPODA-QT networks yielded structurally stable matrices at 37° C.
- **Pre-loaded PPODA-QT:** Direct mixing of Rifampin prior to casting severely stunted total release (<0.1 mg over 144 hrs), indicating the complex drug likely scavenged the thiol-acrylate crosslinking reaction.
- **Post-loaded PPODA-QT:** Swelling blank matrices in a highly concentrated solvent bath proved highly successful. (See Master Graph): This method prevented crosslinking interference, yielding a sustained, gradual diffusion profile delivering a significantly higher payload (~0.75 mg) over a 6-day period.

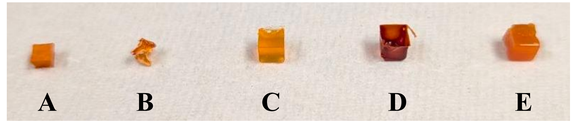

Figure 3: *Fabricated matrix iterations:* ***(A)*** *PLGA-coated Gelatin,* ***(B)*** *PLGA-coated PVA,* ***(C)*** *Pre-loaded PPODA-QT,* ***(D)*** *Hollow PLGA Shells, and* ***(E)*** *Post-loaded PPODA-QT.*

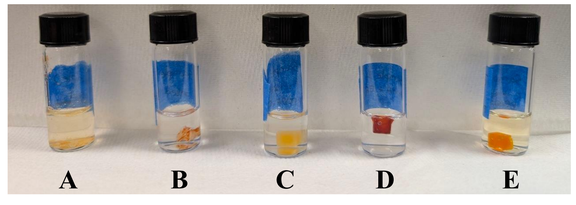

Figure 4: *In vitro structural stability of the evaluated interconnected microparticle arrays (Vials A-E) in PBS at 37° C, highlighting the structural failure of physical hydrogels (A) versus the stability of the optimized synthetic network (E).*

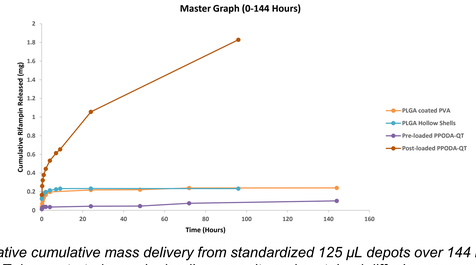

Figure 5: *Comparative cumulative mass delivery from standardized 125 µL depots over 144 hours. Solvent-swelled PPODA-QT demonstrated superior loading capacity and sustained diffusion compared to boundary coatings and hollow shells.*

Results

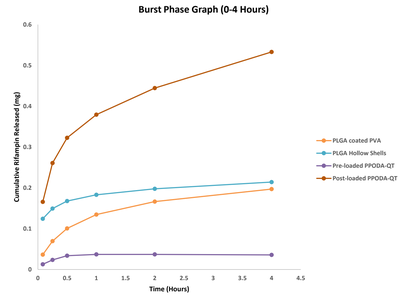

Figure 6: *The 4-hour burst phase inset clearly highlights the rapid initial dose-dumping of the PLGA-coated architectures prior to their premature plateau.*

Summary, Conclusions and Future Directions

- The physical manufacturability of an interconnected microparticle array was successfully validated.
- Uncrosslinked physical hydrogels (gelatin) and thin dip-coatings fail to provide the thermal stability or diffusion bottleneck required for sustained physiological implants.
- Post-loading structurally stable synthetic networks (PPODA-QT) via solvent-swelling successfully prevents crosslinking interference and provides the necessary sustained release profile.

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