

Preclinical Evaluation of Poly(Ester Urea) Nanofiber Envelopes for Sustained Antibiotic Delivery in Orthopaedic Implant-Associated Infections

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INTRODUCTION: Implant related infections are serious complications relevant to orthopaedic surgeries. Especially in open fractures, initial bacterial contamination at the injury site could persist on implant surfaces causing soft tissue damage and hardware failure, as systemic antibiotics often fail to reach effective concentrations locally. This study evaluates a biodegradable nanofiber envelope for sustained local delivery of rifampin and minocycline to prevent implant-associated infections in a laboratory animal model.

METHODS:

In vitro evaluation: Poly(ester urea) (PEU) nanofiber envelopes were fabricated via electrospinning and drug release kinetics were analyzed via high performance liquid chromatography (HPLC), and monitored over 14 days. Scanning electron microscopy (SEM) confirmed nanofiber morphology. Effectiveness of different polymer formulations, fabrication methods, and drug dosings using minocycline (M) and rifampin (R) were measured with Kirby-Bauer disc diffusion assays against *S. aureus* and *S. epidermidis*. The optimized formulation (5% w/w polymer in hexafluoroisopropanol loaded with 10% w/w M and 15% w/w R mixed prior to fabrication, “10M15R”) was selected based on the drug release profile and effectiveness.

In vivo evaluation: Thirty-six New Zealand white rabbits (18 male, 18 female) underwent bilateral subcutaneous implantation of Ti-6AL-4V ELI discs, followed by standardized inoculation with *S. aureus* (10^8 CFU/mL, 0.5 mL per pocket) at implant sites. Animals were randomly assigned to one of three groups with an equal number and gender split: 1) control (bare discs), 2) blank (discs covered in PEU envelopes without antibiotics), and 3) drug (discs covered in 10M15R envelope). Discs were explanted at postoperative days 7 and 14. Infection burden was assessed via culturing of swabs and sonication media for qualitative assessments and quantitative bacteria counts, respectively. Histological assessment is in active preparation.

RESULTS: Among 16 tested antibiotics dosing combinations, 10M15R demonstrated robust in vitro effectiveness with zones of inhibition comparable to higher-dose combinations, supporting its selection as a balanced choice with minimized risk of dose-related side effects. The V8₇₀F6₃₀ PEU with antibiotics mixed prior to fabrication demonstrated consistent dual-antibiotic release over 14 days. In vivo, both control and blank envelope groups showed persistent bacterial growth on days 7 and 14. In contrast, the drug group demonstrated complete eradication of *S. aureus* at both timepoints. Additionally, there were no incidents of skin breakdown or implant extrusion in the drug group, while such complications led to data loss in the control and blank treatments. Additional surgeries are ongoing to restore planned sample sizes for statistical analysis.

DISCUSSION AND CONCLUSION: This PEU nanofiber envelope loaded with rifampin and minocycline provided sustained local antibiotic delivery and demonstrated complete in vivo eradication of *S. aureus* in a rabbit implant infection model. These results support translation toward clinical use for orthopedic implant-related infection prophylaxis.

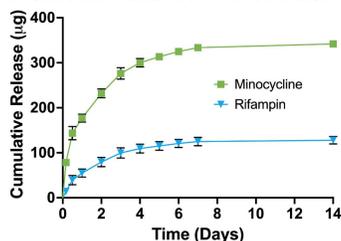


Figure 1 In vitro antibiotics release kinetics of 10M15R

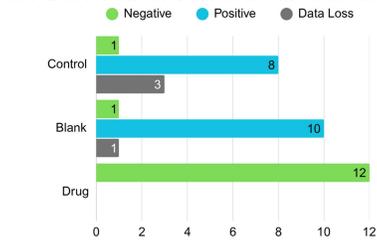


Figure 2 In vivo quantification from swabs of explanted discs. Data from day 7 and 14 are combined. N=12 for each group. Positive is defined as having >1 colony on plates from swabs of the implant site and on implant surface; data loss were from skin breakdown and implant extrusion due to infection

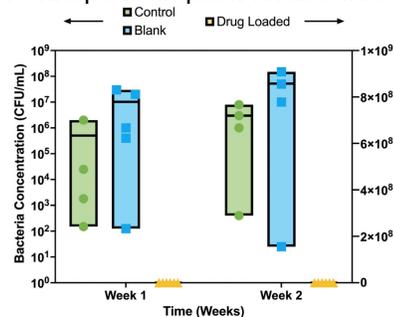


Figure 3 In vivo quantification of infection burden from sonication of explanted discs.