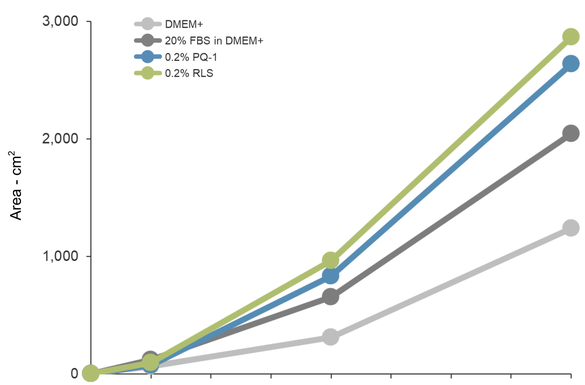
POLYQUATERNIUM-1 AND RHAMNOLIPIDS FOR BIOFILM CONTROL AND HEALING IN CHRONIC WOUND MODELS

Authors: Kelly Strout
Abbey Sells
Organization: Stepan Company
Contact: Kelly.Strout@stepan.com

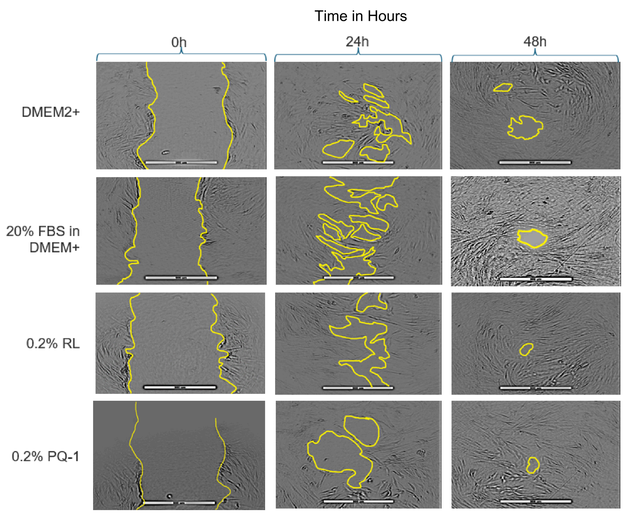
The Challenge: Biofilm-mediated persistent infections sustain inflammation, increase antimicrobial tolerance, and disrupt repair signaling resulting in stalled chronic wound closure.
The Gap: An unmet need persists for host-compatible biofilm control that supports healing while targeting clinically relevant wound pathogens, including MRSA and P. aeruginosa.
Our Approach: Polyquaternium-1 (PQ-1) and fermentation-derived rhamnolipids (RL) deliver multifunctional complementary mechanisms of action. Rapid antibiofilm control with pro-healing support validated through in vitro biofilm and fibroblast assays and in vivo obese diabetic wound model causing impaired healing function with prescribed subset implanted with MRSA biofilm.

✓ Promotes Fibroblast Migration

0.2% PQ-1 and RL improve closure kinetics (extent and rate) relative to negative and positive controls



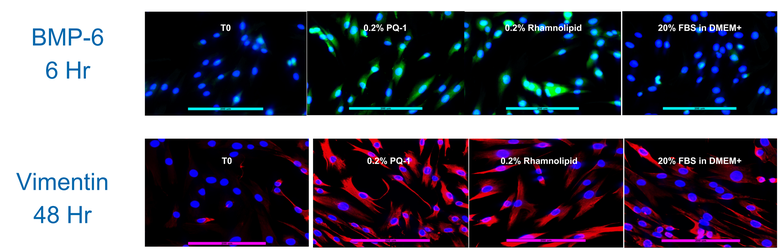
Increased AUC integrates faster closure kinetics with greater total wound infill over time



Method
Human dermal fibroblasts were seeded in 12-well plates and grown to ~90% confluence (N=3/Treatment). A linear scratch was made using a sterile pipette tip, followed by treatment with control or test formulations in DMEM2+. Cultures were incubated under standard conditions for 48 ± 2 hr to assess cell migration and wound closure.

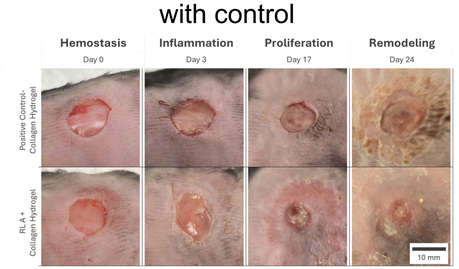
✓ Enhanced Wound-Healing Protein Expression

RL broadly upregulates wound-repair markers, while PQ-1 selectively increases vimentin during repair.

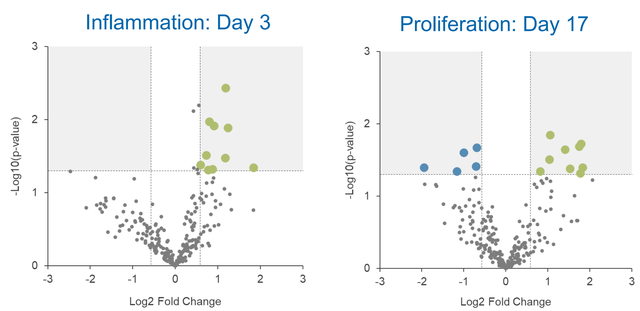


✓ Improves In Vivo Wound Healing

RL reduces time to closure and improved wound-bed quality compared with control



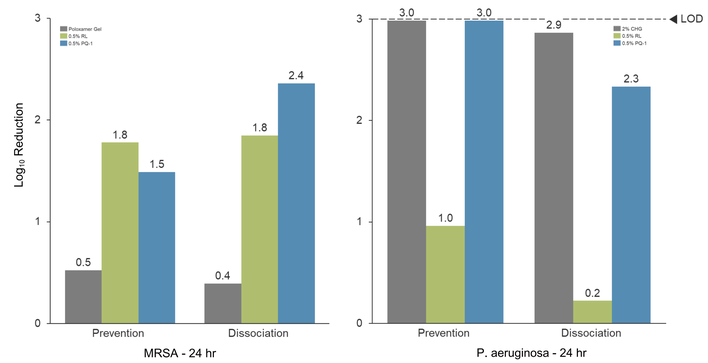
RL beneficially modulates wound healing genes, regulating key areas: inflammation, angiogenesis, and cellular proliferation.



Method:
Diabetic, obese, male mice with 10mm punch biopsy. Treated with 1% rhamnolipid in collagen hydrogel and covered with dressing at indicated time point. NanoString samples collected at Day 3 and Day 17.

✓Demonstrates Infection Control

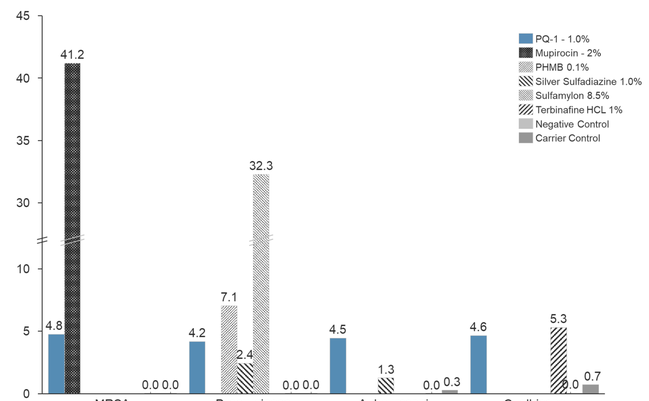
PQ-1 and RL have biofilm prevention and dissociation properties



Method
Prototypes were tested against MRSA and PA biofilms using the Calgary Biofilm Device. Test solutions were applied for 24 hr to assess both prevention and disruption. Biofilms were analyzed by flow cytometry and stained with crystal violet to highlight biofilm.

PQ-1 Demonstrates in vitro Broad-Spectrum Efficacy

Zone of Inhibition



Method:
Agar diffusion plates of TSA with 5% sheep's blood. 10mm punch. 200µl test substance incubated for 24hrs at 37°C and measured using planimetry method.

Conclusion

PQ-1 and rhamnolipids induce an early pro-repair fibroblast response in a scratch-wound model, improving both infill kinetics and total infill. In vivo, rhamnolipids enhance wound healing versus a commercial comparator, integrating host repair modulation with microbial/biofilm control. Together they can provide a complementary dual-function for solution integrating host repair modulation with microbial / biofilm control.

Next Steps

No antagonism was observed in early antimicrobial interaction studies, and both rhamnolipids and PQ-1 were readily formulated in collagen hydrogels, supporting feasibility for topical delivery. Next studies will define dose–response and temporal marker dynamics, validate complementarity in mature/mixed biofilm systems, and confirm efficacy in clinically relevant in vivo wound models, including infected and biofilm-burdened settings.

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Authors: **Kelly Strout**
Abbey Sells
Contact: **Kelly.strout@stepan.com**
Organization: **Stepan Company, Northfield, IL.**

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BACKGROUND: Chronic wounds often fail to close because recalcitrant biofilms sustain inflammation, resist antimicrobials, and impair repair signaling. We evaluated whether polyquaternium-1 (PQ-1) and fermentation-derived rhamnolipids (RLs)—alone and in combination—deliver complementary activity: rapid antimicrobial/biofilm control plus host-compatible, pro-healing responses.
METHODS: Biofilm prevention and dissociation were quantified using the Calgary Biofilm Device against MRSA and Pseudomonas aeruginosa following 24-h exposure, with biofilm readouts by flow cytometry and crystal-violet staining; P. aeruginosa datasets used n=10 replicates (turbidity/flow cytometry). Time-kill assays assessed planktonic reductions (LOD ≥3.0 log) versus buffer/water and chlorhexidine gluconate (CHG). Host-relevant responses were assessed via fibroblast scratch closure and phase-timed wound-healing markers (BMP-6, vimentin). Translation to delayed healing was evaluated in obese diabetic BKS.Cg-Dock7m +/+ Lepr db/J mice (N=36) treated with RL–collagen hydrogel prototypes; wound tissue was profiled at Days 3 and 17 using a 282-gene wound-healing panel, and an infection-challenge arm used 3D-printed Staphylococcus aureus biofilms with fluorescence imaging of tissue burden.
RESULTS: Against MRSA biofilm at 0.5% actives (24 h), RL achieved 1.78-log prevention and 1.85-log dissociation, while PQ-1 achieved 1.49-log prevention and 2.36-log dissociation. Against P. aeruginosa at 0.5% (24 h), RL showed limited activity (≈0.24-log prevention; 0.03-log dissociation), whereas PQ-1 achieved ≥2.27-log prevention (LOD) and 2.06-log dissociation (n=10). At higher concentrations, PQ-1 delivered LOD-limited ≥2.5-log prevention and ≥2.8-log dissociation, while RL improved dissociation to ~1.5-log, consistent with biosurfactant-enabled matrix disruption. In time-kill assays, PQ-1 (≥1.25%) and RL:PQ-1 combinations met the ≥3-log LOD, whereas RL alone yielded ~0.5-log; CHG also met ≥3-log. In scratch assays, RL drove 90–95% closure versus ~95% positive and ~72% negative controls; PQ-1 accelerated early kinetics (T50 23.3 h vs 33.6 h control) with phase-appropriate BMP-6 (6 h) and vimentin (24 h) modulation and no antagonism with RLs. In vivo, RL–collagen hydrogels supported ~7-day sustained release and sterilization stability, accelerated wound closure with improved periwound integrity, and upregulated repair-associated pathways (e.g., remodeling, migration, angiogenesis, proliferation) by gene profiling. In the biofilm-challenge arm, RL hydrogels produced a marked reduction in deep-tissue infection signal by fluorescence imaging.
CONCLUSION: PQ-1 provides broad antimicrobial/biofilm clearance, particularly for P. aeruginosa, while RLs contribute MRSA biofilm control and robust pro-healing genetic and functional responses in a clinically relevant obese diabetic mouse model. Together, they form a dual-modality strategy (infection/biofilm control + tissue repair) that addresses key failure modes in chronic wounds, supporting optimized co-formulation and confirmatory infected-wound translation studies to finalize dose and feasibility.