Peptide-based Biomimetic Matrix Eliminates Multidrug-Resistant Pseudomonas in Complex Ulcers

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BACKGROUND

Current approaches in complex wound management have serious limitations, and the rise of multidrug-resistant organisms (MDROs) and biofilms further complicates treatment[1]. Biofilm infections have been associated with wound chronicity, partly due to promoting a chronic inflammatory environment as well as shielding pathogens from the patient's immune response and from antimicrobial treatments[2]. To address this challenge, we developed a self-assembling peptide **biomimetic matrix (BMM*)** designed to (i) provide antibacterial protection via cationic charge and (ii) facilitate tissue regrowth through a 3D scaffold that mimics the native extracellular matrix (ECM). The purpose of this study was to evaluate the antibacterial and wound healing properties of BMM.

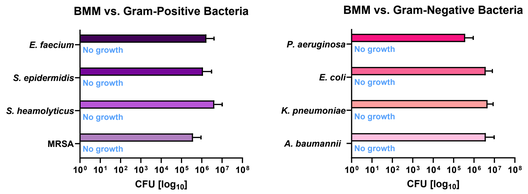
METHODS

Preclinical: Antibacterial efficacy against clinically relevant MDROs was tested *in vitro*. Efficacy against *in vitro* relevant multispecies biofilms and *ex vivo* [porcine skin] 72 hour-aged *Pseudomonas aeruginosa* (PAO1) biofilms was also assessed. MRSA-inoculated murine wounds treated with BMM were monitored by *in vivo* imaging and microbiology. Bacterial cell membrane permeabilization assays were used to confirm BMM's antibacterial mechanism. Compatibility with mammalian cells was evaluated *in vitro* using co-cultures of murine fibroblasts and bacteria. In a swine model of full-thickness excisional wounds, healing was evaluated vs. silver and collagen products using digital imaging and histopathology.

Clinical: Two patients presenting with ulcers secondary to venous disease and complicated by multidrug-resistant Pseudomonas infection that failed to respond to previous advanced treatments (including antimicrobials and spray-on living cells) were selected to receive BMM. BMM was applied post wound preparation, including debridement. The ulcers were monitored for bioburden and healing progress.

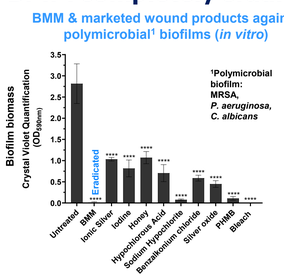
RESULTS

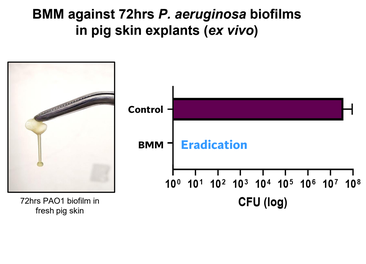
1. BMM demonstrated broad-spectrum antibacterial activity against clinical isolates



- Complete bactericidal activity against 10^6 CFU of Gram-positive & Gram-negative clinical isolates, all multidrug-resistant organisms (MDROs), within 24 hours

2. BMM completely eradicated mature biofilms

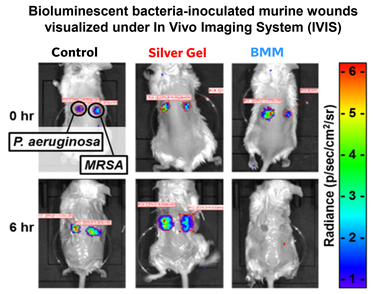


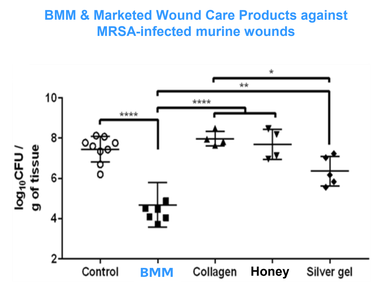


- Complete eradication of established multispecies biofilms *in vitro* within 24 hours
- 72h-aged PAO1 biofilm eradication confirmed in pig skin explants within 24 hours

RESULTS

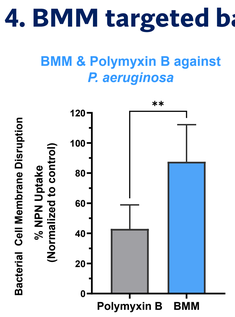
3. BMM substantially reduced *in vivo* wound bioburden

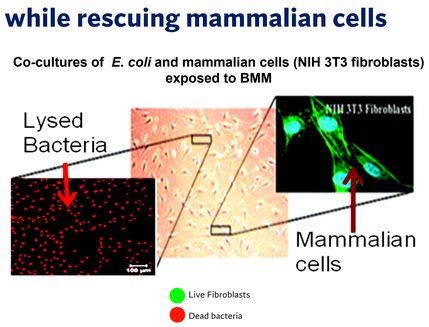




- Elimination of *P. aeruginosa* & MRSA from murine wounds within 6 hours
- Superior wound bioburden reduction compared to tested commercially available wound care products

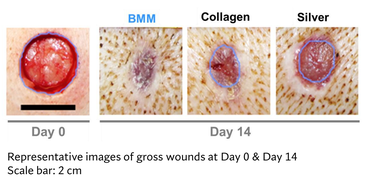
4. BMM targeted bacteria while rescuing mammalian cells



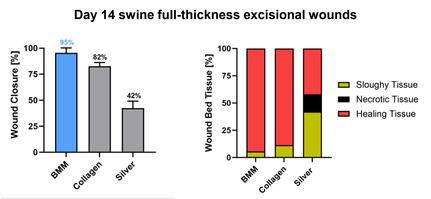


- Bacterial cell membrane disruption capacity superior to antibiotic drug Polymyxin B
- Selective bactericidal activity against microbes and rescue of mammalian fibroblasts
- High mammalian cell viability, cell spreading, and cell attachment

5. BMM improved healing in a swine full-thickness wound model



Representative images of gross wounds at Day 0 & Day 14
Scale bar: 2 cm



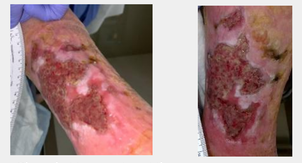
- Superior healing profile compared to collagen and silver with greater wound closure (95% ± 5%), increased granulation tissue, increased neovascularization, and reduced inflammation
- Only treatment achieving complete re-epithelialization by Day 14 post-wounding

RESULTS

6. BMM completely eliminated infection in complex ulcers

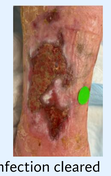
Patient 1. Venous Leg Ulcer, complicated by multidrug-resistant *P. aeruginosa* and MSSA

Presentation / Before BMM



- Chronic Venous Leg Ulcer
- Cultures positive for multidrug-resistant *Pseudomonas aeruginosa* and methicillin-sensitive *Staphylococcus aureus* (MSSA)
- Heavy and persistent drainage

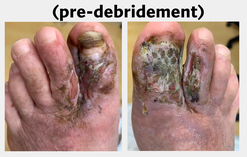
After BMM (2 applications)



- ✓ Bacterial infection cleared (no growth confirmed by cultures)
- ✓ Substantial wound area & volume reduction
- ✓ Clinically meaningful improvement in drainage
- ✓ No adverse events

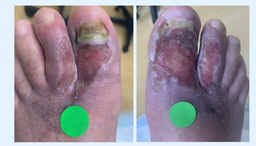
Patient 2. Ulcer secondary to venous disease, complicated by multidrug-resistant *P. aeruginosa*

Presentation (pre-debridement) / Before BMM (post-debridement)



- Ulcer refractory to treatments (antimicrobials & living cells)
- Persistent ABX-resistant infection
- Serous exudate

After BMM (2 applications)



- ✓ Bacterial infection cleared (no growth confirmed by cultures)
- ✓ Substantial wound area reduction
- ✓ Improved drainage
- ✓ No adverse events

SUMMARY & CONCLUSIONS

In vitro, BMM demonstrated broad-spectrum activity against MDROs and established biofilms, while maintaining high cytocompatibility with mammalian fibroblasts. In murine models of infected full-thickness excisional wounds, BMM showed superior bioburden reduction when compared to silver- and honey-based antimicrobial wound products. Clinical outcomes confirmed clearance of multidrug-resistant Pseudomonas infection in refractory venous ulcers and rapid progress towards healing, suggesting benefits in chronic wound management complicated by biofilm infection and a potential change in practice. Further studies are needed to validate and expand the clinical findings.

References:
[1]*Sen CK. Human Wound and Its Burden: Updated 2022 Compendium of Estimates. Adv Wound Care (New Rochelle). 2023 Dec;12(12):657-670. doi: 10.1089/wound.2023.0150. PMID: 37756368; PMCID: PMC10615092.*
[2]*Ding X, Tang Q, Xu Z, Xu Y, Zhang H, Zheng D, Wang S, Tan Q, Maitz J, Maitz PK, Yin S, Wang Y, Chen J. Challenges and innovations in treating chronic and acute wound infections: from basic science to clinical practice. Burns Trauma. 2022 May 21;10:tkac014. doi: 10.1093/burnst/tkac014. PMID: 35611318; PMCID: PMC9123597.*

Note: Preclinical findings may not translate into clinical outcomes in patients.

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