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 through a mechanism that evades microbial resistance and (ii) encourage tissue regrowth through a scaffold that mimics the native extracellular matrix (ECM). The purpose of this study was to evaluate the antibacterial and wound healing properties of BMM in MDRO-infected wounds.

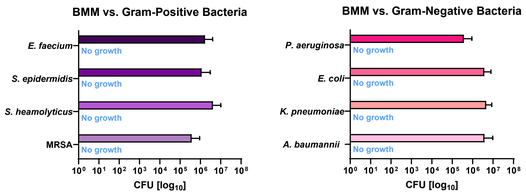
METHODS

Preclinical: Antibacterial efficacy against clinically relevant MDROs was tested in vitro. Bacterial cell membrane disruption studies were conducted to confirm BMM antibacterial mode of action. Efficacy against in vitro multispecies [K. pneumoniae, P. aeruginosa, MRSA] biofilms and ex vivo [porcine skin] 72 hour-aged Pseudomonas aeruginosa (PAO1) biofilms was also assessed. Compatibility with mammalian cells was evaluated in vitro using co-cultures of mammalian fibroblasts and bacteria. MRSA-inoculated murine wounds treated with BMM were monitored by in vivo imaging and microbiology.

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

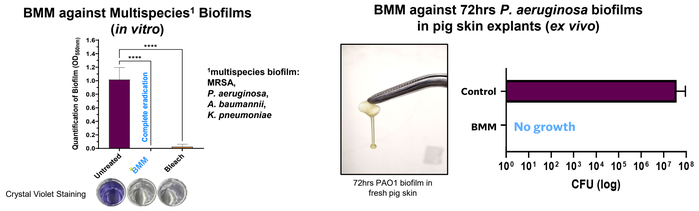
RESULTS

1. BMM demonstrates 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

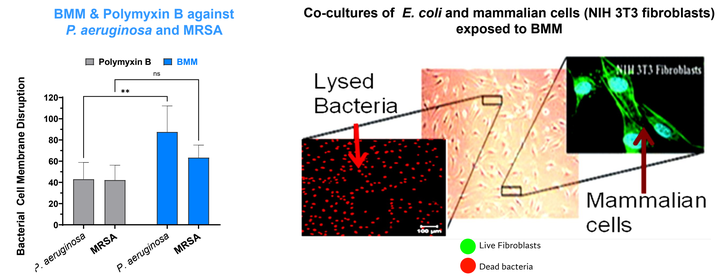
2. BMM completely eradicates mature biofilms



- Complete eradication of mature multispecies biofilms *in vitro*
- 72h-aged PAO1 biofilm eradication confirmed in pig skin explants

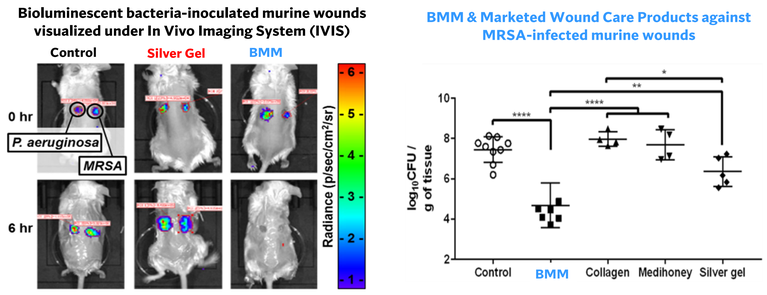
RESULTS

3. BMM antibacterial mode of action selectively targets pathogens and rescues mammalian cells



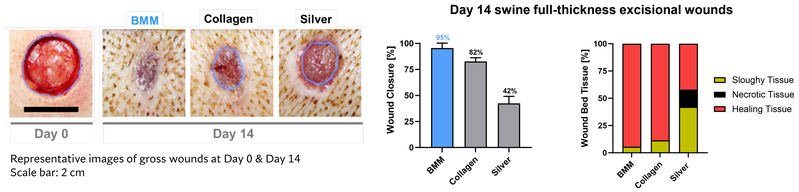
- Antibacterial mode of action targets bacterial cell membranes, minimizing risk of resistance
  Superior bacterial cell membrane disruption compared to antibiotic drug Polymyxin B
- Selective bactericidal activity against microbes and rescue of mammalian fibroblasts
- High mammalian cell viability, cell spreading, and cell attachment

4. BMM substantially reduces *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

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

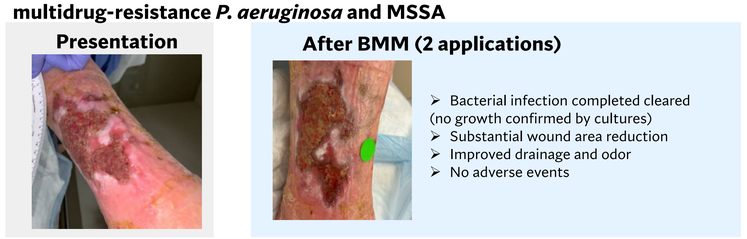


- Superior healing profile compared to collagen and silver with greater wound closure (95% ± 5%), increased granulation tissue, increased neovascularization, and reduced inflammation
- Only treatment achieving complete re-epithelialization by Day 14 post-wounding

RESULTS

6. BMM completely eliminates infection in complex ulcers

Patient 1. Venous Leg Ulcer with persistent heavy drainage, complicated by multidrug-resistance *P. aeruginosa* and MSSA



Patient 2. Venous ulcer refractory to advanced treatments (including living cells), complicated by multidrug-resistance *P. aeruginosa*

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.*

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