Innovative Peptide-Based Technology Facilitates Rapid Closure and Provides Antibacterial Protection of Surgical Wounds

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Introduction

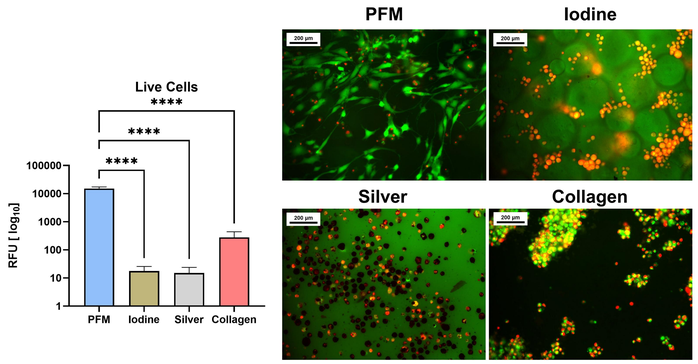
Surgical wound complications, such as surgical wound dehiscence (SWD), represent a leading cause of morbidity following surgery. Prone to occur in high-risk patients, SWD involves the separation of the margins of a closed incision, resulting in increased mortality, prolonged hospital stays, and excess healthcare costs. To address this challenge, **we developed a synthetic peptide flowable matrix** (PFM, Suprello™, Gel4Med Inc.) specifically designed for surgical wounds to control bioburden and promote wound healing.

Methods

Mammalian cell viability, cell attachment, and cell spreading were evaluated after 24-72 hours of exposure to PFM, iodine or silver wound dressings, and hydrolyzed collagen wound product. Efficacy against gram-positive and gram-negative bacteria was assessed using time-kill assays. *In vitro*, efficacy against 72-hour *Pseudomonas aeruginosa* (PAO1) mature biofilms was compared to marketed antimicrobial wound products. PFM wound healing efficacy was tested in a swine model of Methicillin-resistant *Staphylococcus aureus* (MRSA) inoculated in dorsal full-thickness incisional wounds. After the bacterial inoculation, incisions were treated with PFM or an antibiotic-infused collagen surgical product, followed by incision closure. On days 3, 7, and 21 post-incision, sites were excised for histopathological evaluation.

Results

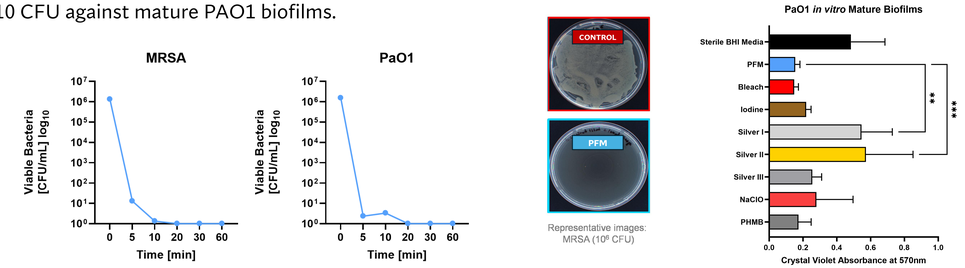
PFM demonstrates higher cell viability ($p<0.0001$, n=3) in mouse fibroblasts when compared to iodine, silver, and hydrolyzed collagen wound products. Compared with other wound products, **superior cell attachment and cell spreading were also observed in PFM-treated cells.**



LIVE/DEAD cell viability assays. CD1 cells (primary mouse embryonic fibroblasts, MEF) were seeded on FloMatrixx and competitors' wound dressings composed of iodine, silver, and collagen. After 24 h, cells were treated with calcein and propidium iodide for fluorescence microscopy. Live cells fluoresce bright green, whereas dead cells with compromised membranes fluoresce red-orange. *Data is shown as mean ± SD. RFU: Relative Fluorescence Units. ****p<0.0001, one-way ANOVA followed by Dunnett's multiple comparisons test.*

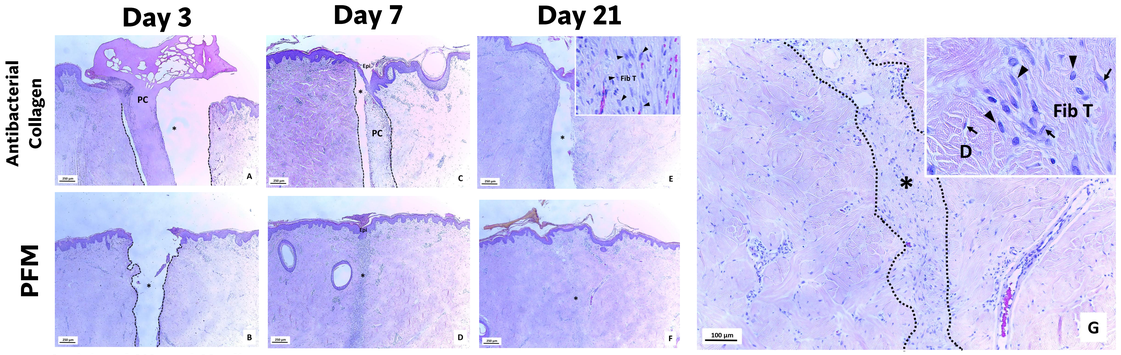
Scan Me!

PFM exhibited strong bactericidal efficacy against 6 log_{10} CFU of PAO1 and MRSA at 5, 10, 15, 30, and 60 minutes, and after 24 hours ($p<0.0001$, n=3). **Compared to marketed antimicrobial dressings, PFM showed superior efficacy** against > 6 log10 CFU against mature PAO1 biofilms.



Antibacterial Activity. (Left) Time-Kill assays of MRSA and PA01. (Right) Performance of PFM compared to commercial antimicrobials dressing. ***p=0.001 and ***p=0.0008. One-way ANOVA followed by Tukey's multiple comparison test.*

PFM achieved incisional wound healing with full reepithelialization, no signs of infection, and total material resorption with complete tissue apposition in 7 days. In contrast, wounds treated with antibacterial collagen showed exuberant incision lines and residual material, resulting in incomplete tissue apposition on day 21.



Incisional Wound Healing. Wounds treated with PFM show full closure, tissue apposition, and complete resorption by day 7, with minimal fibrotic tissue at the incision site, while wounds treated with antibacterial collagen show the presence of occlusive material and incomplete tissue apposition by day 21. **PC**: positive control, antibacterial collagen. *****incision site; **dotted lines**: incision line; **D**: dermis; **Fib T**: fibrotic tissue; **arrows**: fibroblasts; **arrowheads**: macrophages.

Discussion

PFM demonstrates superior cell compatibility and antibacterial and antibiofilm efficacy compared to hydrolyzed collagen and antimicrobial surgical wound products. PFM resulted in rapid tissue integration, complete tissue apposition, and full reepithelialization within 7 days in a swine model of infected incisional wounds. Together, the data support PFM's potential to manage surgical incisions better and prevent surgical wound complications. Clinical studies are needed to validate these findings.