Synthetic Resorbable Antibiofilm Polymeric Wound Matrix Containing Gallium and Silver

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INTRODUCTION

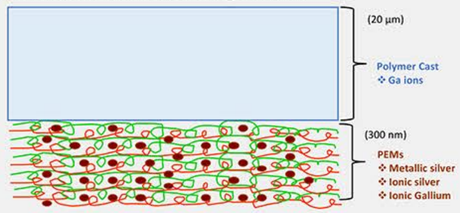
Polymeric microfilm matrix

- ❖Biofilms are bacteria encased in extracellular polymeric substance (EPS)
- ❖Biofilms exist in 60% of chronic wounds, 6% of acute wounds[1]
- ❖Biofilms are diffusive barriers that make bacteria 1000 times more resistant to antibiotics/antimicrobials than planktonic bacteria[2,3]

Goal: To identify combination of **gallium (antibiofilm agent)** and **silver (antimicrobial)** that works synergistically within a **polymeric microfilm** to **disperse biofilms and kill bacteria**.

INNOVATION

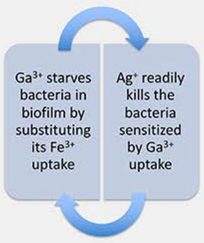
Strategy: Wound surface modification with **synthetic polymer microfilm** that releases **silver and gallium**



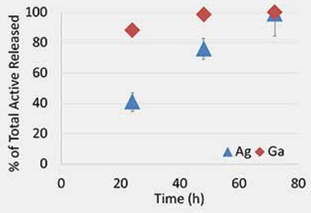
Microfilm consists of two layers

- ❖ Water soluble polymer cast with or without gallium nitrate
- ❖ Polyelectrolyte multilayers (PEMs) matrix containing ionic silver and gallium and metallic silver

Antibiofilm Gallium and Antimicrobial Silver

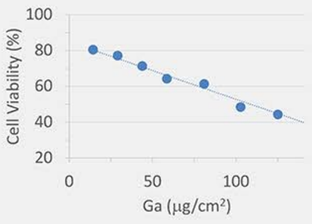


- ❖ Gallium ***replaces iron needed for metabolism*** due to its chemical similarities[4,5]
- ❖ Gallium cannot be reduced under physiological conditions[4,5]
- ❖ Gallium ***blocks redox-driven biological processes of metabolism*** that reduces bacterial growth and biofilm formation[4,5]
- ❖ 10 µg/cm² silver in PEMs
- ❖ 5-105 µg/cm² gallium in microfilm



Films extracted in simulated wound fluid (SWF, 1x MEM with 10% FBS) at 37˚C

- ❖ Burst release of gallium as polymer cast dissolves
- ❖ Sustained release of silver as silver nanoparticles dissolve

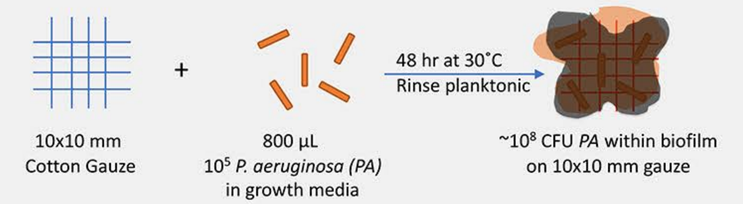


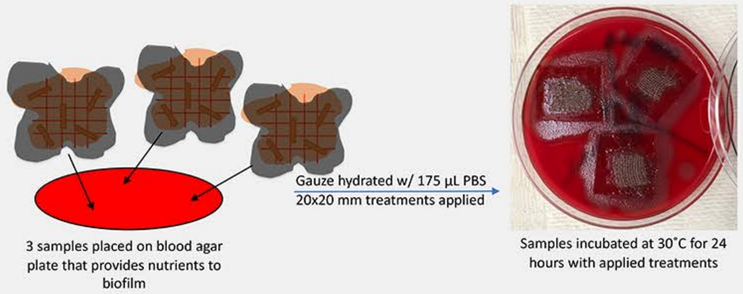
MTT Cytotoxicity Test

- ❖ Gallium in microfilm extracted in SWF at 37˚C for 24 hours
- ❖ Extract dosed on L929 mouse fibroblasts for 24 hours at 37˚C
- ❖ 62% cell viability at 70 µg/cm² gallium
- ❖ Dose limits of gallium 0-125 µg/cm²

METHODS

Samples evaluated in-vitro against 48-hr old mature biofilms grown on cotton gauze



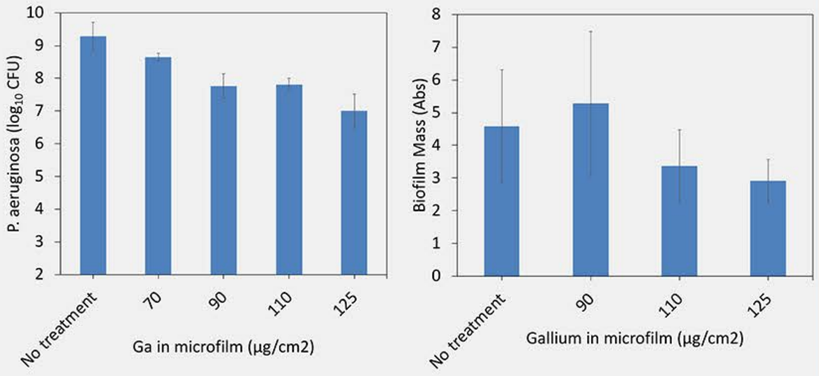


Post treatment, biofilms supported on gauze were rinsed free of planktonic bacteria and transferred to clean well plates.

- ❖ Samples stained with crystal violet and absorbance (@395 nm wavelength) read as a representation of biofilm mass
- ❖ Samples homogenized and serial plated to quantify *P. aeruginosa* colony forming units (CFU)

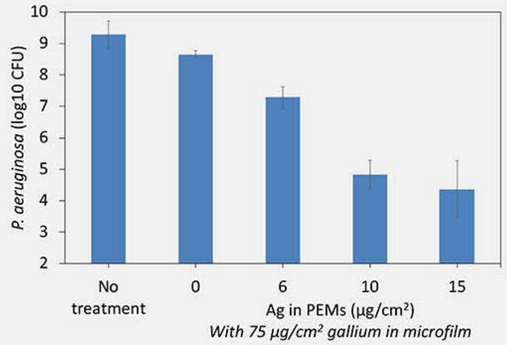
RESULTS

❖ **With no silver in microfilm**



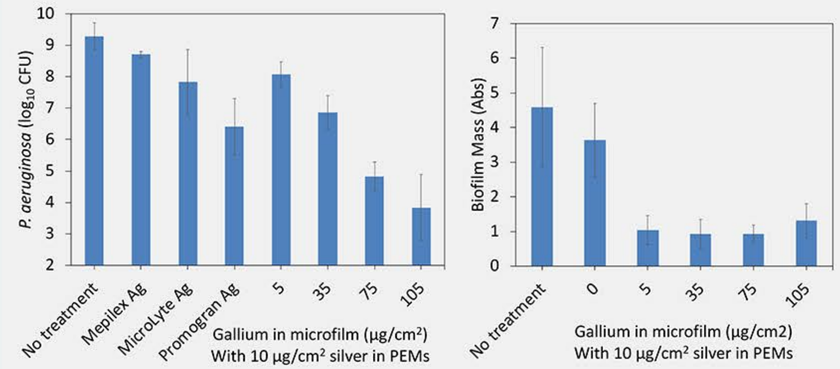
- ❖ Gallium alone is ineffective at reducing bacteria contained within biofilm
  - Limited to ***0.6 ± 0.4 log₁₀ reduction*** of *P. aeruginosa* with ***70 µg/cm² gallium in microfilm***
- ❖ Gallium alone is ineffective at dispersing biofilm mass
  - Achieved ***less than 25% biofilm mass dispersal*** with up to ***125 µg/cm² gallium in microfilm***

❖ **With 75 µg/cm² gallium in microfilm, varied silver quantity within PEMs layer**



✓ With ***addition of silver*** to 75 µg/cm² of gallium, ***>4.5 ± 0.6 log₁₀ CFU reduction to P. aeruginosa can be achieved***

❖ **With 10 µg/cm² of silver in PEMs, varied gallium level in microfilm.**



✓ 10 µg/cm² silver and 5 µg/cm² gallium in microfilm achieves ***>80% biofilm mass dispersal***

✓ When microfilm contains more than 35 µg/cm² gallium the prototype ***reduces more viable bacteria encased in biofilms than commercial silver products***

CONCLUSIONS

Gallium has limited effectiveness against bacteria contained in biofilms at nontoxic doses → Silver has limited effectiveness against bacteria contained in biofilms at nontoxic doses → Silver and gallium together can achieve >4log10 reduction and disperse 80% biofilm mass at benign doses

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(5) Herron, Maggie, et al. "Interfacial Stacks of Polymeric Nanofilms on Soft Biological Surfaces That Release Multiple Agents." *ACS Applied Materials & Interfaces*, 8(40) 2016:26541.