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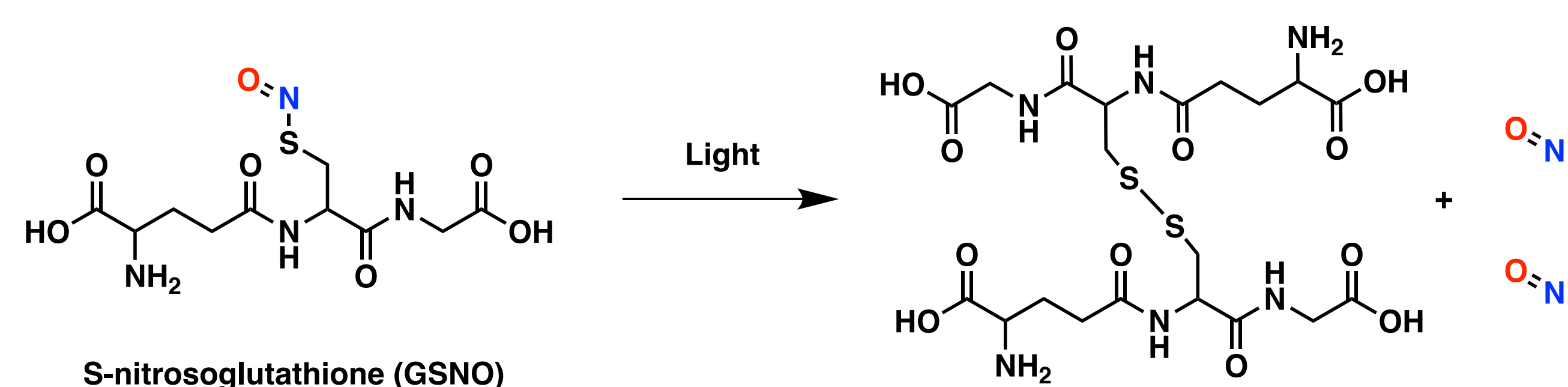
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Background

- Over 5 million central venous catheters (CVCs) are used annually in the US.
- Approximately 250,000 catheter-related bloodstream infections (CRBSIs) occur in the US every year, greatly contributing to morbidity, mortality, and healthcare costs.
- Lock solutions containing high concentrations of antibiotics or antiseptics are clinically used to prevent and/or treat CRBSIs with limited success.
- CRBSIs are associated with biofilm production, which is a major barrier to traditional treatments.
- Nitric oxide (NO) is a potent, endogenous antimicrobial agent that can disperse biofilms, making its incorporation into lock solutions ideal.

S-nitrosoglutathione (GSNO) dissolved in PBS is used as a NO-releasing lock solution (NOreLS).



Scheme 1: NO donor molecules such as GSNO release NO.

NO Release Characterization

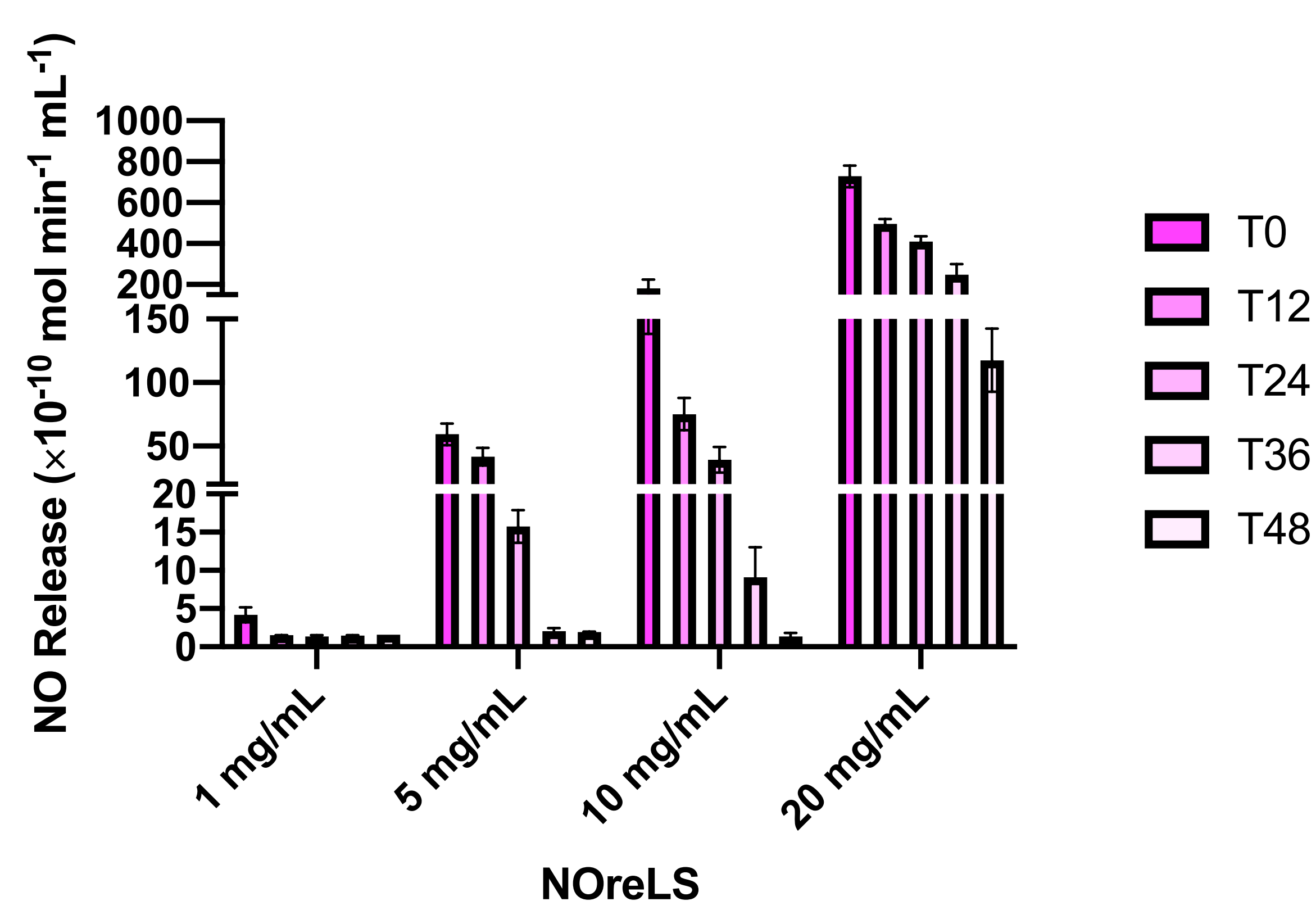


Figure 1: NO analysis demonstrates that all concentrations of GSNO in PBS tested release NO for at least 48 h.

Antibacterial Assessment

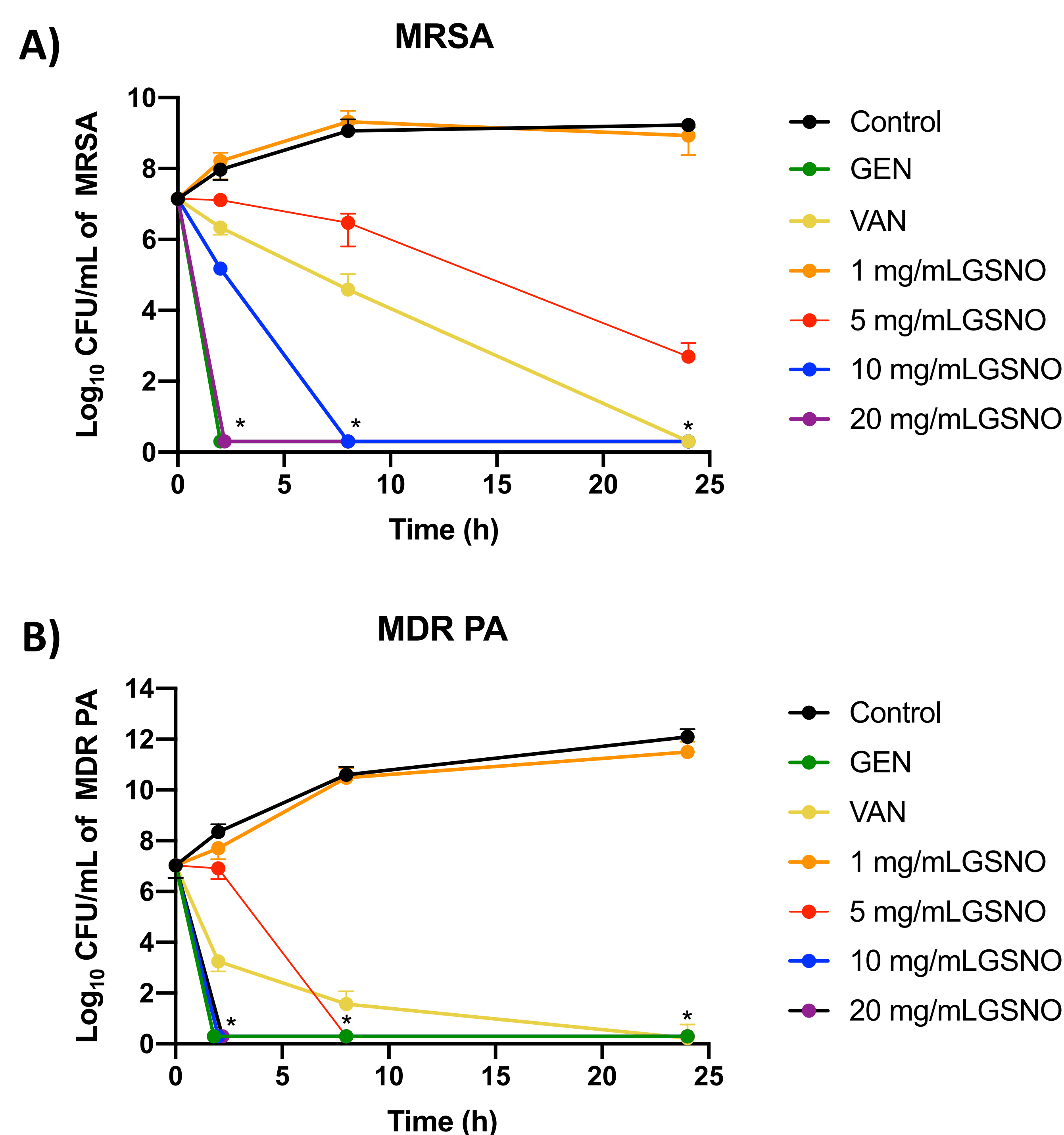


Figure 2: Time kill assays with **A)** methicillin-resistant *Staphylococcus aureus* (MRSA) and **B)** multidrug resistant *Pseudomonas aeruginosa* (MDR PA).

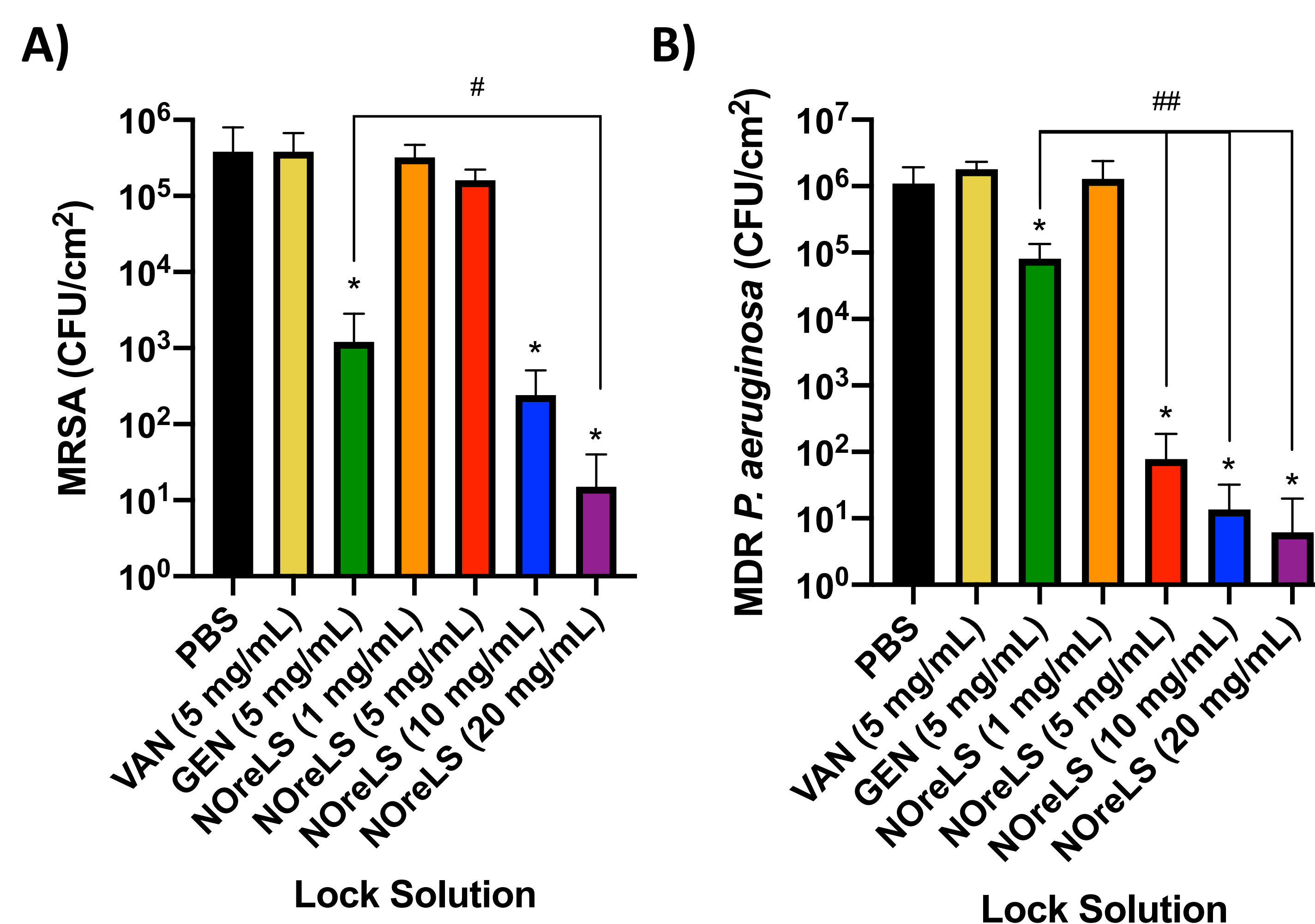


Figure 3: Medical grade tubing was infected for 24 h prior to 2 h lock therapies. Viable **A)** MRSA and **B)** MDR PA on the tubing after treatment.

Biofilm Dispersion

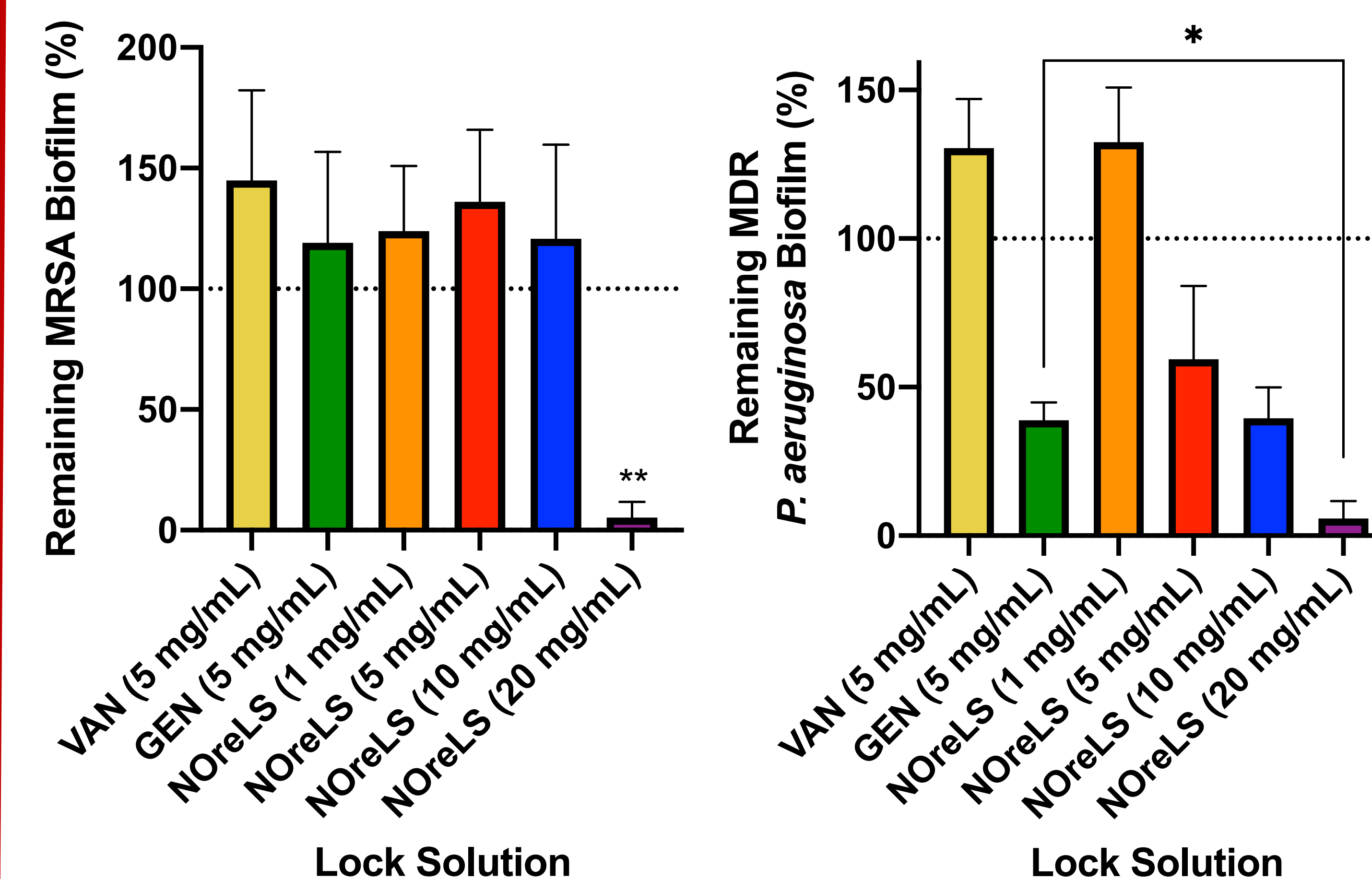


Figure 4: Medical grade tubing was infected for 72 h with media changes every 12 h before 24 h lock treatments. **A)** MRSA and **B)** MDR PA biofilm dispersal was evaluated using crystal violet staining compared to a PBS control.

Cytocompatibility

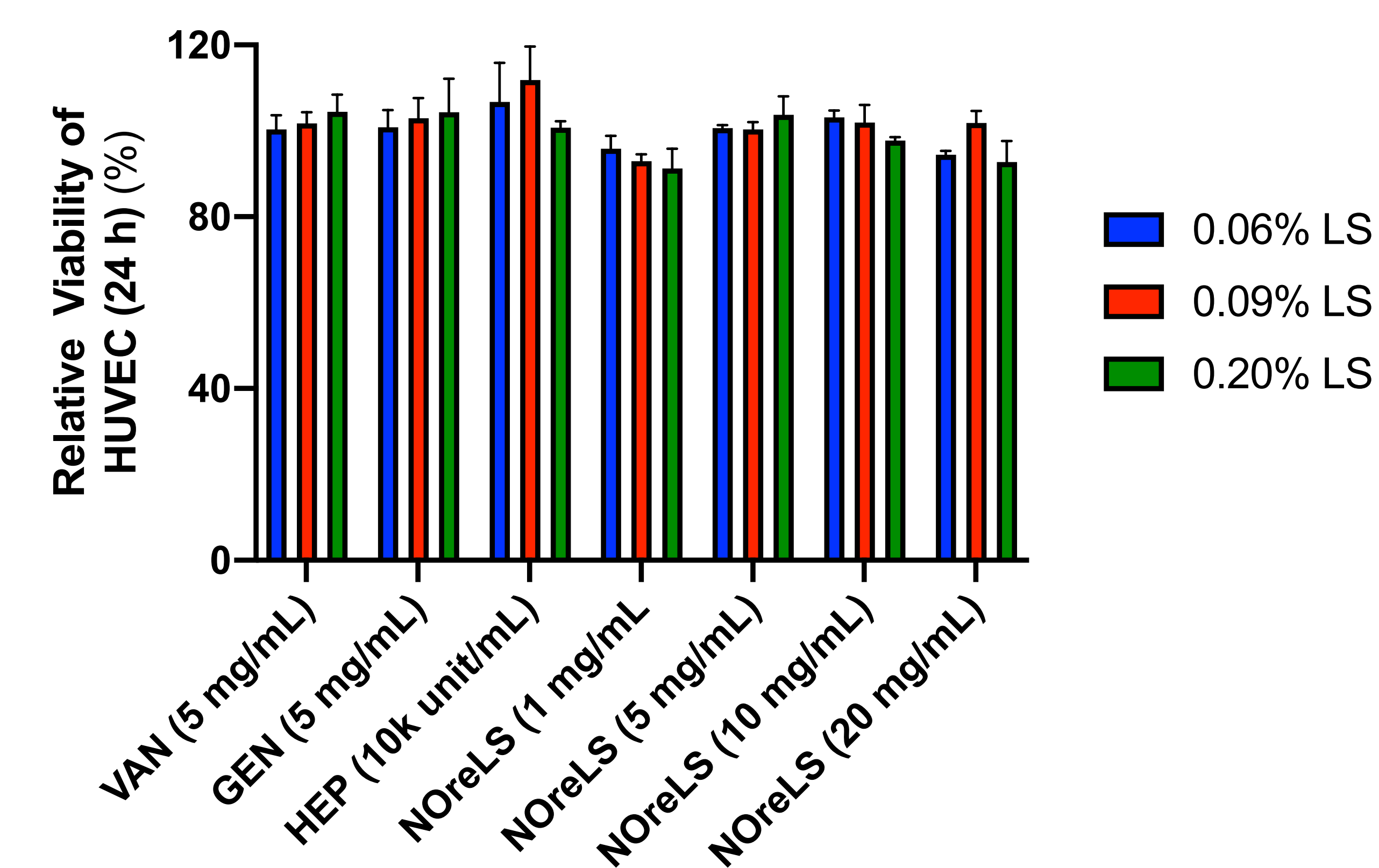


Figure 5: Cytocompatibility assessed via CCK-8 assay. 0.06%, 0.09%, and 0.2% correspond to 3, 4.5, and 10 mL of potentially leaked locked solution into 5 L of blood.

Conclusions

- NOreLS shows highly efficient antibacterial actions for the potential prevention and treatment of CRBSIs.
- At all tested concentrations, NOreLS has been shown to have excellent cytocompatible.
- NOreLS has great potential for clinical translation.

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