**Introduction**

*Staphylococcus aureus* is an important human pathogen causing chronic infections that are difficult to treat. Biofilm contributes to the persistence of infections, by protecting bacteria from immune system and antimicrobial agents. We showed that many antibiotics are poorly active on biofilms [1], especially when using clinical isolates from persistent infections [2]. Fusidic acid (FUS) may constitute a useful alternative for treatment of *Staphylococcus aureus* infections (in regions with low resistance rates) but shows moderate activity against biofilm constituents.

**Materials and Methods**

*S. aureus* reference strain ATCC25923 and 5 clinical strains isolated on medical devices or from chronic tissue infections were used. Biofilms were grown for 24 h in 96-wells plates and then exposed for 48 h to increasing concentrations (0.25-200 µg/mL) of FUS (to obtain full concentration-response curves), combined with concentrations corresponding to the human IC₅₀ or the IC₉₀ of the associated drug. Bacterial viability in biofilms was quantified using the redox indicator resazurin (reduced to fluorescent resorufin by viable bacteria); biofilm biomass was evaluated using crystal violet absorbance.

**Results**

Combining FUS at IC₉₀ with daptomycin (DAP), vancomycin (VAN), or linezolid (LDZ) improved in general its efficacy, with reduction in viability reaching globally 75-96% when these companion drugs were used at their IC₉₀.

**Conclusions**

Combining FUS with DAP, VAN, or LDZ appears as a useful strategy to increase its antibacterial activity against biofilms. These data support the evaluation of these combinations in biofilm-related infections in vivo.

### References


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**Fig 1**: % reduction in viability within biofilms for antibiotics alone or for FUS at IC₉₀ combined with other antibiotics at their respective IC₉₀/IC₉₀. Reduction in viability was compared to untreated control. FUS IC₉₀ 3.5 mg/L; DAP IC₉₀/IC₉₀ 0.7/8.4 mg/L; VAN IC₉₀/IC₉₀ 2.5/20 mg/L; LDZ IC₉₀/IC₉₀ 9/17 mg/L.

**Fig 2**: Concentration-response curves for a typical clinical isolate (80124430375) Viability (% control values) in biofilms exposed to FUS alone over a wide range of conc. (blue); fC₉₀ of DAP/VAN/LDZ alone (green) or in combination with FUS at increasing conc. (black).