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In vitro Activity of TNP-2092 against Biofilms Formed by Prosthetic Joint Infection-Associated Staphylococci

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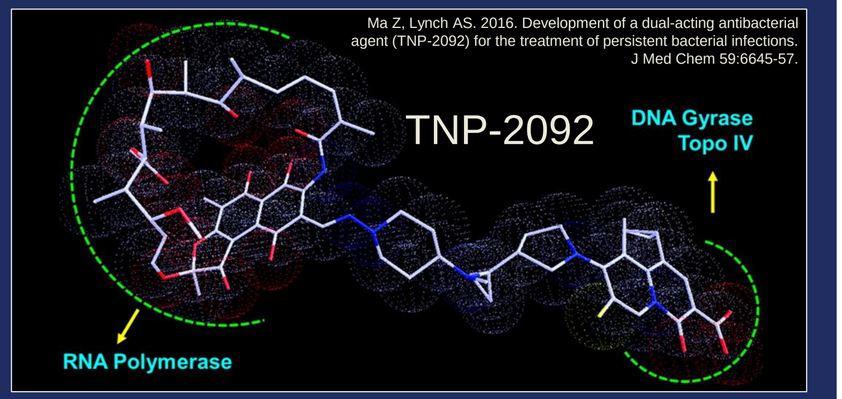
Background

Staphylococci, including both *Staphylococcus aureus* and *Staphylococcus epidermidis*, are the most common cause of prosthetic joint infection (PJI). (1). TNP-2092 is an investigational drug composed of rifamycin and quinolizinone pharmacophores conjugated via a stable linker. Here, we determined TNP-2092's *in vitro* activity against biofilm state PJI-associated methicillin-susceptible *S. aureus* (MSSA), methicillin-resistant *S. aureus* (MRSA), methicillin-susceptible *S. epidermidis* (MSSE) and methicillin-resistant *S. epidermidis* (MRSE) compared to ciprofloxacin and rifampin alone, alongside other anti-staphylococcal antimicrobial agents.



Methods

Isolates Used: 20 MRSA, MSSA, MRSE, and MSSE (80 total)

Antimicrobials Studied:

- TNP-2092
- Rifampin
- Ciprofloxacin
- Ciprofloxacin + 1μg/ml Rifampin
- Daptomycin
- Vancomycin

Minimum Biofilm Inhibitory Concentration (MBIC) (4)**:**

- Bacteria grown to 0.5 McFarland in tryptic soy
- Aliquots transferred to 96-well flat-bottom plates with 96-pegged lids
- Plates incubated on a shaker for 5 hrs at 37℃
- Lids rinsed in PBS and placed into serial 2-fold drug dilution plates
- Incubated for 24 hrs at 37℃.
- **MBICs were read by visual turbidity.**

Minimum Biofilm Bactericidal Concentration (MBBC) (4)**:**

- After MBIC, lids rinsed with PBS and placed onto CAMHB plates
- Incubated for 24 hours at 37℃.
- **MBBCs determined by visual turbidity**.

Results

Figure 1. Cumulative percent susceptibility of ***S. aureus*** for minimum biofilm inhibitory concentration (MBIC) (A), and minimum biofilm bactericidal concentration (MBBC) (B).

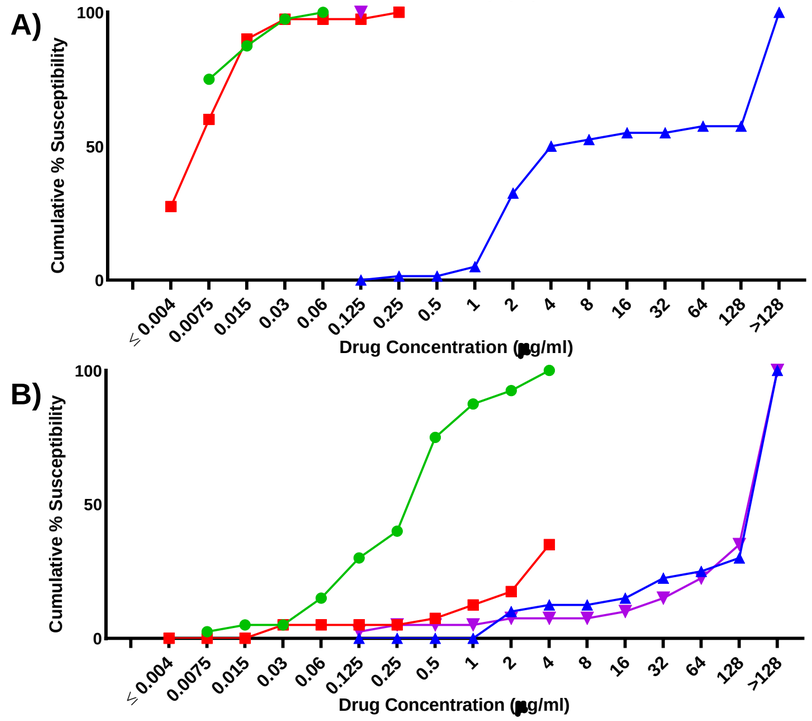
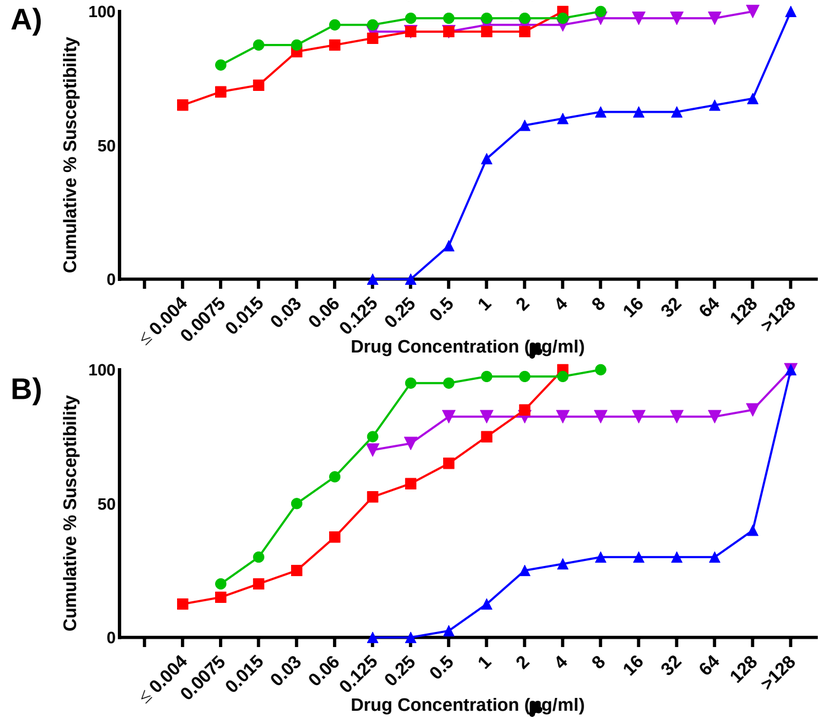


Figure 2. Cumulative percent susceptibility of ***S. epidermidis*** for minimum biofilm inhibitory concentration (MBIC) (A), and minimum biofilm bactericidal concentration (MBBC) (B).



TNP-2092 (0.0075 - 8μg/ml) | Rifampin (0.004 - 4μg/ml) | Ciprofloxacin (0.125 - 128μg/ml) | Ciprofloxacin + 1 μg/ml Rifampin (0.125 - 128μg/ml)

Discussion

- TNP-2092 inhibitory and bactericidal activity against biofilm-state staphylococci was equivalent or superior to rifampin
- Bactericidal antagonism was observed between ciprofloxacin and rifampin during combinational treatment
- Hybrid antimicrobial agents may have clinical treatment potential

Conclusions

TNP-2092 has promising *in vitro* activity against biofilm-state PJI-associated staphylococci.

References

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Acknowledgements

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