The Fluorocycline TP-271 is Potent Against Major Complicated Community-Acquired Bacterial Pneumonia (CABP) Pathogens
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Abstract
A greater than 60-year track record of proven safety and clinical success validates the tetracyclines as a valuable class of broad-spectrum antibiotics worthy of continued drug development. Tetracyclines arrest the growth of bacteria by blocking the binding of aminoacyl-RNA to the A site of the 30S ribosomal subunit. While antibacterial activity is generally considered bacteriostatic, it has been shown that tetracyclines can be bactericidal in some cases, with some organisms [1, 2]. TP-271 is a novel, fully synthetic fluorocycline antibacterial in preclinical development for IV/local treatment of moderate to severe respiratory infections caused by susceptible and multidrug-resistant (MDR) public health and biothreat pathogens [3].

Introduction

Methods

Results

Table 1. Determination of MIC50 and MIC90 values for CABP Pathogens

<table>
<thead>
<tr>
<th>Organism</th>
<th>MIC50 (µg/mL)</th>
<th>MIC90 (µg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td>0.03-0.25</td>
<td>0.12-1.0</td>
</tr>
<tr>
<td><em>Haemophilus influenzae</em></td>
<td>0.5-4</td>
<td>1-8</td>
</tr>
<tr>
<td><em>Streptococcus pneumoniae</em></td>
<td>0.03-0.25</td>
<td>0.12-1.0</td>
</tr>
<tr>
<td><em>Mycoplasma pneumoniae</em></td>
<td>0.03-0.25</td>
<td>0.12-1.0</td>
</tr>
</tbody>
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Figure 1. Time Kill Curves for CABP Pathogens

Conclusions

TP-271, a novel fully synthetic tetracycline, exhibited excellent potency against key MDR public health respiratory pathogens, including *S. pneumoniae*, MRSA, *S. pyogenes*, *H. influenzae*, and *M. catarrhalis*. TP-271 showed good activity against atypical pathogens *M. pneumoniae*, *L. pneumophila*, and *C. pneumoniae*, however, in vitro activity against the latter two organisms was likely limited by media interference, and thus potency is underestimated in these assays.

TP-271 was generally bacteriostatic against MRSA, *S. pneumoniae*, *S. pyogenes*, and *M. catarrhalis* at 4X and 8X MIC. At 2 µg/mL, an estimation of the CB50 in man, TP-271 showed bactericidal activity against some isolates.

TP-271 was bacitracin-resistant against *H. influenzae* in all concentrations tested.

TP-271 shows promise as a new antibiotic for the empirical treatment of moderate-to-severe CABP.

Table 2. Media used in *C. pneumoniae* and *L. pneumophila* assays in combination with TP-271 activity

<table>
<thead>
<tr>
<th>Compound</th>
<th>MIC50 (µg/mL)</th>
<th>MIC90 (µg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C. pneumoniae</td>
<td>0.03-0.25</td>
<td>0.12-1.0</td>
</tr>
<tr>
<td>L. pneumophila</td>
<td>0.03-0.25</td>
<td>0.12-1.0</td>
</tr>
</tbody>
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References

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