Antimicrobial Activity of CEM-101 a New Macrolide, Tested Against Diverse Collections of Bacterial Biowarfare/Bioterrorism Agents

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Abstract

Background: There continues to be a feared scenario of terrorist attacks with aerosolized microorganisms leading to mass infections. Given the increased possibility of resistance to current treatments through genetic engineering or natural emergence, identifying effective antibiotics with novel mechanisms of action is critical to counter such an attack. In this study, we determined the minimum inhibitory concentrations (MICs) of a new macrolide CEM-101 against genotypic and geographic diverse collections of five BW/BT agents: Bacillus anthracis, Yersinia pestis, Burkholderia mallei, and B. pseudomallei.

Methods: Inoculum preparation and antibiotic microdilution were performed according to CLSI methods. MICs for 30 strains of each agent were determined by the microdilution method in 96-well plates, after an 18- or 42-h incubation at 35°C.

Results: CEM-101, MIC ranges, MIC₅₀, and MIC₉₀ (µg/ml) were: B. anthracis 0.008-0.015, 0.008, 0.008, Y. pestis 0.25-2, 1, 2, F. tularensis <0.08-4, 0.03, 2, B. mallei 0.25-2, 1, 1, and B. pseudomallei 16, 16, 16.

Conclusions: CEM-101 a new macrolide antibiotic had significant in vitro activity against many of the biowarfare/bioterrorism (BW/BT) agents tested, with the exception of the Burkholderia strains. It has been shown that many macrolides preferentially accumulate intracellularly, which may enhance efficacy when used as a postexposure prophylaxis for preventing pneumatic disease among individuals exposed to aerosolized BW/BT agents. The potential broad-spectrum activity along with oral bioavailability makes CEM-101 an attractive candidate for treating BW/BT exposures and infections. Efficacy of CEM-101 in the animal-infection models for these agents should be evaluated.

Background

There continues to be a feared scenario of battlefield use or terrorist attacks with aerosolized microorganisms leading to mass infections. Adding the very real possibility of resistance to current treatments through genetic engineering or natural emergence, identifying effective antibiotics which are able to overcome resistance to current approved drugs or have novel mechanisms of action is critical. CEM-101 is a new macrolide that has demonstrated activity against macrolide-resistant bacteria and is more active than azithromycin or clarithromycin against macrolide-resistant bacterial strains. In this study, we determined the minimum inhibitory concentrations (MICs) of CEM-101 against genotypic and geographic diverse collections of five biowarfare/bioterrorism agents: Bacillus anthracis, Yersinia pestis, Francisella tularensis, Burkholderia mallei and B. pseudomallei.

Results

CEM-101 Minimum Inhibitory Concentration Distributions

<table>
<thead>
<tr>
<th>Species</th>
<th>MIC₅₀ (µg/ml)</th>
<th>MIC₉₀ (µg/ml)</th>
<th>MIC₅₀ (µg/ml)</th>
<th>MIC₉₀ (µg/ml)</th>
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<tr>
<td>B. anthracis</td>
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<td>0.015</td>
<td>0.008</td>
<td>0.008</td>
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<tr>
<td>Y. pestis</td>
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<td>2</td>
<td>0.03</td>
<td>2</td>
</tr>
<tr>
<td>F. tularensis</td>
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<td>4</td>
<td>0.03</td>
<td>2</td>
</tr>
<tr>
<td>B. mallei</td>
<td>0.25</td>
<td>2</td>
<td>0.03</td>
<td>2</td>
</tr>
<tr>
<td>B. pseudomallei</td>
<td>16</td>
<td>16</td>
<td>16</td>
<td>16</td>
</tr>
</tbody>
</table>

Conclusions

CEM-101 a new macrolide antibiotic had significant in vitro activity against many of the biowarfare/bioterrorism agents tested, with the exception of the Burkholderia strains. It has been shown that many macrolides preferentially accumulate intracellularly, which may enhance efficacy when used as a postexposure prophylaxis for preventing pneumatic disease among individuals exposed to aerosolized BW/BT agents. The potential broad-spectrum activity along with oral bioavailability makes CEM-101 an attractive candidate for treating BW/BT exposures and infections. Efficacy of CEM-101 in the animal-infection models for these agents should be evaluated.

References


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