**CHIR-090**

**Cat. No.:** HY-15460  
**CAS No.:** 728865-23-4  
**Molecular Formula:** C₂₄H₂₇N₃O₅  
**Molecular Weight:** 437.49

**Target:** Bacterial  
**Pathway:** Anti-infection

**Storage:**  
- Powder: -20°C, 3 years; 4°C, 2 years  
- In solvent: -80°C, 6 months; -20°C, 1 month

**Solvent & Solubility**

**In Vitro**  
DMSO: ≥ 30 mg/mL (68.57 mM)  
*"≥" means soluble, but saturation unknown.*

<table>
<thead>
<tr>
<th>Preparing Stock Solutions</th>
<th>Solvent Concentration</th>
<th>1 mg</th>
<th>5 mg</th>
<th>10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 mM</td>
<td>2.2858 mL</td>
<td>11.4288 mL</td>
<td>22.8577 mL</td>
</tr>
<tr>
<td></td>
<td>5 mM</td>
<td>0.4572 mL</td>
<td>2.2858 mL</td>
<td>4.5715 mL</td>
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<tr>
<td></td>
<td>10 mM</td>
<td>0.2286 mL</td>
<td>1.1429 mL</td>
<td>2.2858 mL</td>
</tr>
</tbody>
</table>

Please refer to the solubility information to select the appropriate solvent.

**In Vivo**

1. CHIR-090 is prepared in 0.04% DMSO^{[3]}.

**BIOLOGICAL ACTIVITY**

**Description**  
CHIR-090 is a potent, slow, tight-binding inhibitor of the LpxC deacetylase. It binds to *E. coli* LpxC with a *Kᵢ* of 4.0 nM.

**IC₅₀ & Target**  
*Kᵢ*: 4 nM (*Escherichia coli* LpxC)^{[3]}  

**In Vitro**  
CHIR-090 is a potent, slow, tight-binding inhibitor of the LpxC deacetylase from the hyperthermophile *Aquifex aeolicus*, and it has excellent antibiotic activity against *P. aeruginosa* and *E. coli*, as judged by disk diffusion assays. CHIR-090 is also a two-step slow, tight-binding inhibitor of *Escherichia coli* LpxC with *Kᵢ*=4 nM. CHIR-090 at low nM levels inhibits LpxC orthologues from diverse Gram-negative pathogens, including *Pseudomonas aeruginosa*, *Neisseria meningitidis*, and *Helicobacter pylori*. In contrast, CHIR-090 is a relatively weak competitive and conventional inhibitor (lacking slow, tight-binding kinetics) of LpxC from *Rhizobium leguminosarum* (*Kᵢ*=340 nM), a Gram-negative plant endosymbiont that is resistant to this compound. An *E. coli* construct in which the chromosomal
lpxC gene is replaced by R. leguminosarum lpxC is resistant to CHIR-090 up to 100 μg/mL, or 400 times above the minimal inhibitory concentration for wild-type E. coli. CHIR-090, a very potent, slow, tight-binding inhibitor of Aquifex aeolicus LpxC, the sequence of which is 31% identical to E. coli LpxC. CHIR-090 has remarkable antibiotic activity against E. coli and P. aeruginosa, comparable to ciprofloxacin, as judged by disk diffusion assays[1].

<table>
<thead>
<tr>
<th>In Vivo</th>
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<tbody>
<tr>
<td>CHIR-090 is a potent antibiotic against E. coli and inhibits E. coli LpxC activity in vitro in the low nM range. E. coli W3110 colonies resistant to 1 μg/mL CHIR-090 are not observed without prior chemical mutagenesis. A strain of E. coli W3110 is able to grow on LB agar plates containing 1 to 10 μg/mL CHIR-090, which is 4 to 40 times above the MIC of 0.25 μg/mL under our conditions for wild-type E. coli W3110. The doubling time of W3110RL is 40 min in the presence of 1 μg/mL CHIR-090, which is exactly the same rate as wild-type in the absence of inhibitor. Wild-type cells stopped growing after about 2 h in the presence of 1 μg/mL CHIR-090[1].</td>
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</tbody>
</table>

PROTOCOL

**Kinase Assay [1]**

Disk diffusion is conducted, except that 10 μg of each antibiotic compound is used per filter. Growth in liquid medium in the presence of CHIR-090 is evaluated as follows: cells from overnight cultures are inoculated into 50 mL portions of LB broth at an A_{600} of 0.02 and grown with shaking at 30°C. When the A_{600} reaches 0.15, parallel cultures are treated with either 6 μL of 500 μg/mL CHIR-090 in DMSO or 6 μL of DMSO. To assess cumulative growth, cultures are maintained in log phase growth by 10-fold dilution into pre-warmed medium, containing the same concentrations of DMSO or DMSO/CHIR-090, whenever the A_{600} reaches 0.4. The minimal inhibitory concentration is defined as the lowest antibiotic concentration at which no measurable bacterial growth is observed in LB medium containing 1% DMSO (v/v), when inoculated at a starting density of A_{600}=0.01. Cultures are incubated with shaking for 24 h at 30°C in the presence of CHIR-090. Experiments are performed in triplicate[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- **Nature.** 2018 Jul;559(7713):259-263.

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REFERENCES


