**BIological Activity:**

CHIR-090 is a two-step slow, tight-binding inhibitor of *Escherichia coli* LpxC with $K_i$ of 4 nM.

IC50 & Target: $K_i$: 4 nM (*Escherichia coli* LpxC)\(^1\)

**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 $K_i$: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* ($K_i$: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\(^1\).

**In Vivo:** 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*. 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\(^1\).

**Protocol (Extracted from published papers and Only for reference)**

**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\(^1\).

**References:**


Caution: Product has not been fully validated for medical applications. For research use only.

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