Ganfeborole hydrochloride

Cat. No.: HY-107775

CAS No.: 2131798-13-3

Molecular Formula: $C_{10}H_{14}BCl_2NO_4$

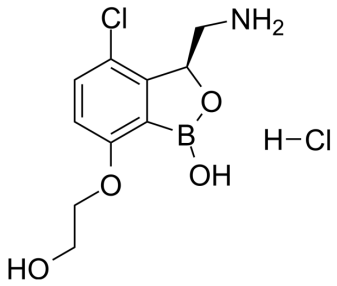
Molecular Weight: 293.94

Target: Bacterial

Pathway: Anti-infection

Storage: 4°C, sealed storage, away from moisture

* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 67.5 mg/mL (229.64 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	3.4021 mL	17.0103 mL	34.0205 mL
	5 mM	0.6804 mL	3.4021 mL	6.8041 mL
	10 mM	0.3402 mL	1.7010 mL	3.4021 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (8.51 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (8.51 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (8.51 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Ganfeborole hydrochloride (GSK656) is a potent antitubercular agent, acting as an inhibitor of Mycobacterium tuberculosis (*Mtb*) leucyl-tRNA synthetase (LeuRS), with an IC_{50} of 0.2 μM.

IC_{50} & Target

IC50: 0.2 μM (Mtb LeuRS)[1]

In Vitro

Ganfeborole hydrochloride is highly selective inhibitor for Mycobacterium tuberculosis (Mtb) leucyl-tRNA synthetase (LeuRS), with an IC_{50} of 0.2 μM, and shows IC_{50}s of >300 μM and 132 μM for human mitochondrial LeuRS and human cytoplasmic LeuRS, respectively. Ganfeborole hydrochloride exhibits antitubercular activity with minimal inhibitory concentration (MIC) of 80 nM against Mtb H37Rv. Ganfeborole hydrochloride also exhibits EC_{50}s of 381 μM against HepG2

	cell, and 137 μM against HepG2 protein synthesis[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Ganfeborole hydrochloride shows potent antitubercular activity in mice infected with M. tuberculosis H37Rv, with ED_{99} of 0.4 mg/kg[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	HepG2 (HB-8065) cells are cultured with fresh medium (essential minimum Eagle medium, EMEM, supplemented with 5% fetal calf serum and 2 mM l-glutamine) the day before subculturing the plates. On the day of the assay, cells (10 000 cells/well) are seeded in a black 96-well collagen coated microplate with clear bottom, except in column 11, which is dispensed only 100 mL of culture medium. Stock solution from GSK656 is prepared in 100% DMSO. Ten serial 1:2 dilutions are prepared of GSK656, and finally, a 1:200 dilution is made, in medium, to achieve a final concentration of 0.5% of DMSO. Resazurin tablets are dissolved in phosphate buffer saline at a concentration of 0.0042%. After 24 h of incubation of the cells (37°C, 5% CO_2, 95% relative humidity), a volume of 150 μL of culture medium containing the appropriate test concentrations of GSK656 dilutions is added to cells in two replicates. Only 150 μL of 0.5% DMSO is added as blank control. Then, cells are exposed to GSK656 for 48 h. After that, medium is removed and resazurin solution is added to each well and incubated for further 1.5 h. Fluorescence is measured at an excitation wavelength of 515 nm and an emission wavelength of 590 nm in a Microplate reader 1420 Multilabel HTS counter, Victor 2[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice[1] Specific pathogen-free, 8- to 10-week-old female C57BL/6 mice are allowed to acclimate for 1 week. In brief, mice are intratracheally infected with 100 000 CFU/mouse of M. tuberculosis H37Rv. GSK656 is administered for 8 consecutive days starting 1 day after infection. For the chronic assay, mice are intratracheally infected with 100 CFU/mouse and GSK656 administered daily (7 days a week) for 8 consecutive weeks starting 6 weeks after infection. Lungs are harvested 24 h after the last administration, and all lung lobes are aseptically removed, homogenized, and frozen. Homogenates are plated onto 10% OADC-Middlebrook 7H11 medium and incubated for 21 days at 37°C. GSK656 is administered by intravenous route at 5 mg/kg single dose in saline and by oral gavage at 30 mg/kg single dose in 1% methylcellulose (1% MC). For iv route aliquots of 15 μL of blood are taken from the lateral tail vein by puncture from each mouse (n = 3) at 5, 15, and 30 min and 1, 2, 4, 8, and 24 h postdose; for oral route aliquots of 15 μL of blood are taken from the lateral tail vein by puncture from each mouse (n = 3) at 15, 30, and 45 min and 1, 2, 4, 8, and 24 h postdose[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Antimicrob Agents Chemother. 2022 Aug 15;e0060122.
- ACS Chem Biol. 2021 Dec 15.

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REFERENCES

[1]. Li X, et al. Discovery of a Potent and Specific M. tuberculosis Leucyl-tRNA Synthetase Inhibitor: (S)-3-(Aminomethyl)-4-chloro-7-(2-hydroxyethoxy)benzo[c][1,2]oxaborol-1(3H)-ol (GSK656). J Med Chem. 2017 Oct 12;60(19):8011-8026.

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

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