

Product Data Sheet

Product Name: GSK656

Cat. No.: GC32189

Chemical Properties

Cas. No. 2131798-13-3

SMILES OCCOC1=CC=C(Cl)C2=C1B(O)O[C@@H]2CN.[H]Cl

Formula $C_{10}H_{14}BCl_2NO_4$ M.Wt 293.94

Solubility DMSO : 67.5 mg/mL (229.64 mM) Storage Store at -20°C

General tips For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.

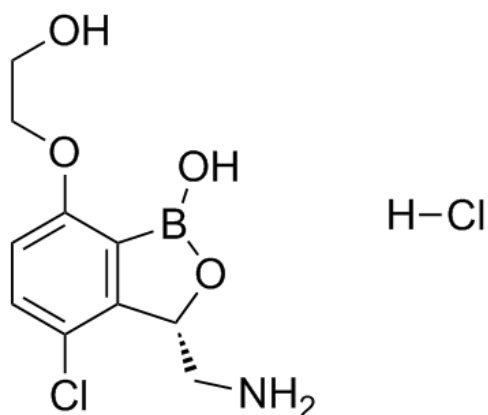
Caution: Product has not been fully validated for medical applications. For research use only.

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Structure



Protocol

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Cell experiment: 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 μ L 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% CO₂, 95% relative humidity), a volume of 150 μ L of culture medium containing the appropriate test concentrations of GSK656 dilutions is added to cells in two replicates. Only 150 μ L 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].

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**Animal
experiment:**

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].

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.

Background

GSK656 is a potent antitubercular agent, acting as an inhibitor of *Mycobacterium tuberculosis* (Mtb) leucyl-tRNA synthetase (LeuRS), with an IC₅₀ of 0.2 µM.

GSK656 is highly selective inhibitor for *Mycobacterium tuberculosis* (Mtb) leucyl-tRNA synthetase (LeuRS), with an IC₅₀ of 0.2 µM, and shows IC₅₀s of >300 µM and 132 µM for human mitochondrial LeuRS and human cytoplasmic LeuRS, respectively. GSK656 exhibits antitubercular activity with minimal inhibitory concentration (MIC) of 80 nM against Mtb H37Rv. GSK656 also exhibits EC₅₀s of 381 µM against HepG2 cell, and 137 µM against HepG2 protein synthesis[1].

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GSK656 shows potent antitubercular activity in mice infected with *M. tuberculosis* H37Rv, with ED99 of 0.4 mg/kg[1].

[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.

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