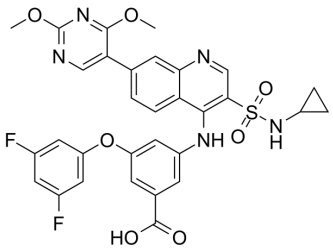
GSK2837808A

Cat. No.:	HY-100681
CAS No.:	1445879-21-9
Molecular Formula:	$C_{31}H_{25}F_2N_5O_7S$
Molecular Weight:	650
Target:	Lactate Dehydrogenase
Pathway:	Metabolic Enzyme/Protease
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (76.92 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.5385 mL	7.6923 mL	15.3846 mL
	5 mM	0.3077 mL	1.5385 mL	3.0769 mL
	10 mM	0.1538 mL	0.7692 mL	1.5385 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 (3.85 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

GSK2837808A is a potent and selective lactate dehydrogenase A (LDHA) inhibitor with IC_{50}s of 2.6 and 43 nM for hLDHA and hLDHB, respectively.

IC_{50} & Target

IC50: 2.6 nM (hLDHA), 43 nM (hLDHB)[1]

In Vitro

GSK2837808A rapidly and profoundly inhibits lactate production rates in multiple cancer cell lines including hepatocellular and breast carcinomas. The potency of GSK2837808A across 30 cancer cell lines with different LDHA and LDHB expression levels ranges from 400 nM to no effect (EC_{50} reported as 30 μM). GSK2837808A potency does not correlate with LDHA, LDHB, or the total LDH expression levels. GSK2837808A inhibits lactate production in hypoxia but at higher concentrations than in normoxia (EC_{50}=10 μM). It also reduces ECAR with EC_{50}=10 μM. LDH inhibition by GSK2837808A alters multiple metabolic pathways in Snu398 cells[1].

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

In Vivo	Clearance following IV infusion of GSK2837808A at 0.25 mg/kg is shown to be 69 mL/minute/kg in rats, which exceeds the animal liver blood flow. Oral dosing of GSK2837808A at 50 mg/kg in rats or 100 mg/kg in mice results in blood compound levels at or below the detection limit of 2.5 ng/mL[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	Sixty thousand Snu398 cells per well are plated in 6-well tissue culture plates in RPMI-1640 medium supplemented with 2.5% charcoal-stripped FBS. Cells are allowed to attach overnight and then DMSO control or the indicated doses of LDHA inhibitor dissolved in DMSO are added directly to the wells. After 4 to 8 days of incubation in the indicated oxygen conditions, adherent cells are trypsinized, counted, and had their viability assessed by the trypan-blue exclusion method using the Vi-Cell XR Cell Viability Analyzer[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice: GSK2837808A is administered to male CD mice or male Sprague-Dawley rats orally or by intravenous (IV) infusion over 120 minutes into a femoral vein. Arterial blood samples are collected over time and GSK2837808A concentration is determined by liquid chromatography (LC)/MS/MS analysis[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Nat Commun. 2020 Jul 9;11(1):3427.
- Nat Commun. 2020 Jun 22;11(1):3162.
- Nat Commun. 2019 Jun 20;10(1):2701.
- J Exp Clin Cancer Res. 2021 Dec 10;40(1):390.
- Clin Transl Med. 2021 Jun;11(6):e467.

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REFERENCES

[1]. Billiard J, et al. Quinoline 3-sulfonamides inhibit lactate dehydrogenase A and reverse aerobic glycolysis in cancer cells. Cancer Metab. 2013 Sep 6;1(1):19.

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