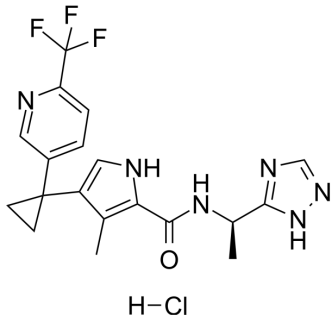
DSM705 hydrochloride

Cat. No.:	HY-132171A
CAS No.:	2989908-08-7
Molecular Formula:	$C_{19}H_{20}ClF_3N_6O$
Molecular Weight:	440.85
Target:	Dihydroorotate Dehydrogenase; Parasite
Pathway:	Metabolic Enzyme/Protease; Anti-infection
Storage:	-20°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

Methanol : 250 mg/mL (567.09 mM; Need ultrasonic)
DMSO : 100 mg/mL (226.83 mM; Need ultrasonic)

Preparing Stock Solutions

Concentration \ Solvent \ Mass	1 mg	5 mg	10 mg
1 mM	2.2683 mL	11.3417 mL	22.6835 mL
5 mM	0.4537 mL	2.2683 mL	4.5367 mL
10 mM	0.2268 mL	1.1342 mL	2.2683 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 (5.67 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.67 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.67 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

DSM705 hydrochloride, an orally active antimalarial compound, is a pyrrole-based Dihydroorotate Dehydrogenase (DHODH) inhibitor. DSM705 hydrochloride exhibits nanomolar potency against Plasmodium DHODH and Plasmodium parasites (IC_{50} =95, 52 nM for P. falciparum and P. vivax DHODH, respectively), with no inhibition of mammalian DHODHs[1].

IC_{50} & Target

Plasmodium

In Vitro

DSM705 hydrochloride shows inhibitory activity against P. falciparum DHODH (PfDHODH, IC_{50}=95 nM), P. vivax DHODH (Pv DHODH, IC_{50}=52 nM) and Pf3D7 cells (EC_{50}=12 nM), with no inhibition of the human enzyme[1].

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

In Vivo

DSM705 (3-200 mg/kg; p.o. twice a day for 6 days) hydrochloride provides the maximum rate of parasite killing at the dose of 50 mg/kg and fully suppresses parasitemia by days 7-8[1].

DSM705 (2.6 and 24 mg/kg; a single p.o.) hydrochloride exhibits high oral bioavailability (74%, 70%), apparent $t_{1/2}$ (3.4, 4.5 h) and C_{max} (2.6, 20 μM) in Swiss outbred mice[1].

DSM705 (2.3 mg/kg; a single i.v.) hydrochloride exhibits plasma clearance (CL=2.8 mL/min/kg) and V_{ss} (1.3 L/kg) in mice[1].

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

Animal Model:	SCID mice were inoculated with parasites[1]
Dosage:	3, 10, 20, 50, 100, 200 mg/kg
Administration:	P.o. twice a day for 6 days
Result:	Killed parasite in a dose dependent manner and fully suppressed parasitemia by days 7-8.

Animal Model:	Swiss Outbred Mice[1]
Dosage:	2.6 and 24 mg/kg for p.o.; 2.3 mg/kg for i.v. (Pharmacokinetic Analysis)
Administration:	A single p.o. and i.v.
Result:	P.o.: F=74/70%, $t_{1/2}$=3.4/4.5 h, C_{max}=2.6/20 μM. I.v.: CL=2.8 mL/min/kg, V_{ss}=1.3 L/kg.

REFERENCES

[1]. Palmer MJ, et, al. Potent Antimalarials with Development Potential Identified by Structure-Guided Computational Optimization of a Pyrrole-Based Dihydroorotate Dehydrogenase Inhibitor Series. J Med Chem. 2021 May 13;64(9):6085-6136.

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