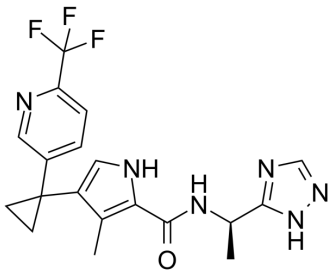
DSM705

Cat. No.:	HY-132171
CAS No.:	2653225-38-6
Molecular Formula:	$C_{19}H_{19}F_3N_6O$
Molecular Weight:	404.39
Target:	Dihydroorotate Dehydrogenase; Parasite
Pathway:	Metabolic Enzyme/Protease; Anti-infection
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	DSM705 is a pyrrole-based Dihydroorotate Dehydrogenase (DHODH) inhibitor. DSM705 exhibits nanomolar potency against Plasmodium DHODH and Plasmodium parasites, with no inhibition of mammalian DHODHs. DSM705 is a potent antimalarial compound[1].
IC_{50} & Target	IC50: 95 nM (P. falciparum DHODH), 52 nM (P. vivax DHODH)[1]
In Vitro	DSM705 shows inhibitory activity against P. falciparum DHODH (PfDHODH, IC_{50}=95 nM), P. vivax DHODH (PvDHODH, 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) 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.) 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.) 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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