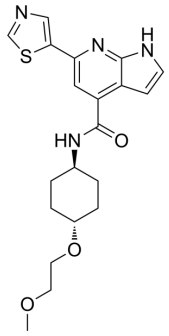
MK-0159

Cat. No.:	HY-150508
CAS No.:	2641484-61-7
Molecular Formula:	$C_{20}H_{24}N_4O_3S$
Molecular Weight:	400.49
Target:	CD38
Pathway:	Immunology/Inflammation
Storage:	4°C, sealed storage, away from moisture and light * In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture and light)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (249.69 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.4969 mL	12.4847 mL	24.9694 mL
	5 mM	0.4994 mL	2.4969 mL	4.9939 mL
	10 mM	0.2497 mL	1.2485 mL	2.4969 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 (6.24 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.24 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

MK-0159 is an orally active, potent and selective CD38 inhibitor, with IC_{50} values of 22, 3, and 70 nM for human, mouse and rat CD38, respectively. MK-0159 also shows good microsomal stability for human and rodent liver microsomes. MK-0159 increases NAD^+ (nicotinamide adenine dinucleotide) and reduces ADPR (adenosine diphosphate ribose) in whole blood and heart[1].

IC_{50} & Target

IC_{50}: 3 nM (mouse CD38), 22 ± 5 nM (hCD38), 70 nM (rat CD38)[1]

In Vitro

MK-0159 (compound 37) (0-50 μM, 24 h) increases both extracellular and intracellular NAD+ in A549 cells and HMVEC cells[1].
MK-0159 (20 μM, overnight) reduces the number of cells with damaged mitochondria in CD38-overexpressing CD8+ T cells[2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

MK-0159 (3-30 mg/kg, p.o., a single dose) increases systemic NAD^+ and decreases ADPR levels (the product and substrate of CD38 enzymatic activity) in blood and heart of mice[1].
MK-0159 (30 mg/kg, p.o.) reduces infarct size in cardiac I/R injury mice[2].
MK-0159 (30 mg/kg, oral gavage, twice a day for 9 days) reverses mitochondrial defect, restores CD8+ T cell function and inhibits virally induced organ inflammation in BXD2 lupus-prone mice with LCMV infection[2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Cardiac I/R injury mice[1]
Dosage:	30 mg/kg
Administration:	p.o.
Result:	Reduced infarct size, and the combination of MK-0159 and NAD+ precursor significantly reduced the infarct size compared to MK-0159 alone. Increased whole heart NAD+ levels and decreased ADPR in the heart.

REFERENCES

[1]. Lagu B, et al. Orally Bioavailable Enzymatic Inhibitor of CD38, MK-0159, Protects against Ischemia/Reperfusion Injury in the Murine Heart. J Med Chem. 2022 Jun 28.

[2]. Chen PM, et al. CD38 reduces mitochondrial fitness and cytotoxic T cell response against viral infection in lupus patients by suppressing mitophagy. Sci Adv. 2022 Jun 17;8(24):eabo4271.

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