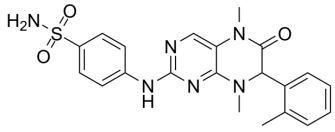
IHMT-MST1-58

Cat. No.:	HY-151257
CAS No.:	2414484-25-4
Molecular Formula:	$C_{21}H_{22}N_6O_3S$
Molecular Weight:	438.5
Target:	Hippo (MST)
Pathway:	Stem Cell/Wnt

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (228.05 mM; ultrasonic and warming and heat to 80°C)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.2805 mL	11.4025 mL	22.8050 mL
5 mM	0.4561 mL	2.2805 mL	4.5610 mL
10 mM	0.2281 mL	1.1403 mL	2.2805 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 (5.70 mM); Clear solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (5.70 mM); Clear solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: 2.5 mg/mL (5.70 mM); Clear solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

IHMT-MST1-58 is a potent, selective mammalian and orally active STE20-like protein 1 kinase (MST1) inhibitor with IC_{50} value of 23 nM. IHMT-MST1-58 can be used for the research of Type 1/2 diabetes[1].

IC_{50} & Target

MST1
23 nM (IC_{50})

In Vitro

IHMT-MST1-58 (compound 19) shows good activity against MST1 with an IC_{50} value of 23 nM[1].

IHMT-MST1-58 (1 μM) displays strong inhibitory activity against MST1 (IC_{50} = 23 nM), weak activity against MST2 (IC_{50} = 652 nM), but no activity against NEK3 even at 10 μM (IC_{50} > 10 μM) [1].

IHMT-MST1-58 (1 μM) shows strong binding affinity to MST1 and weak binding affinity to MST2 with K_d values of 240 nM and 2.7 μM[1].

IHMT-MST1-58 (0.1-10 μM; 1-2 h) inhibits the phosphorylation of MST1 in vitro[1].

IHMT-MST1-58 (0.03, 0.1 and 0.3 μM; 48 h) exhibits a significant protective effect of β cells from the damage caused by inflammatory cytokines[1].

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

Western Blot Analysis[1]

Cell Line:	HepG2 liver cells, RAW264.7, RPE1 and HL7702 cells; INS-1 and RIN-m5F cell lines
Concentration:	0-10 μM
Incubation Time:	2 h (HepG2 liver cells, RAW264.7, RPE1, and HL7702 cells)
Result:	Inhibited the H2O2-stimulated MOB1 phosphorylation and MST1/2 autophosphorylation in a dose-dependent manner in all four cell lines. Inhibited the phosphorylation of LATS1 (T1079) and YAP (S127) in HepG2 cells. Showed strong inhibition of MST1 phosphorylation and its downstream MOB1 autophosphorylation in a dose-dependent manner in both cell lines.

In Vivo

IHMT-MST1-58 (compound 19) (p.o, 50 mg/kg/day, QD) combination with metformin led to the decline of fasting blood glucose, show protective effect of β cells and decrease the hemoglobin A1c level in the STZ-induced T1D/T2D mouse models [1].

Pharmacokinetic Parameters of IHMT-MST1-58 in different species (i.v. or p.o; 1 mg/kg, 5 mg/kg and 10 mg/kg)[1].

	mice		rats		beagle dogs	
parameter	i.v.(1 mg/kg)	p.o.(10 mg/kg)	i.v.(1 mg/kg)	p.o.(10 mg/kg)	i.v.(1 mg/kg)	p.o.(10 mg/kg)
AUC_{0-t}(ng/mL*h)	501.1	5583	2553±155.1	4858±2648	764.5±82.9	4939±1067
$t_{1/2}$(h)	1.7	1.81	3.51±0.34	3.03±0.2	6.47±0.71	5.79±1.09
C_{max}/F (ng/mL)	1240	1922	944.0±219.1	1717±276	466.7±45.2	1113±417
F(%)	-	110.8	-	73.3±40.1	-	106.5±20.9

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Animal Model:	mice[1]
Dosage:	50 mg/kg
Administration:	oral, single
Result:	parameter / plasma / pancreas C_{max}(ng/mL) / 3990±390 / 12216±1509

AUC_{0-t}(ng/mL*h)	13621±2127	51394±10098
Cl(mL/h/kg)	3734±641	996±189

Animal Model:	T1D mouse models and T2D mouse models[1]
Dosage:	50 mg/kg
Administration:	p.o, 50 mg/kg/day, QD
Result:	Decreased the FBG level, improved the food intake and water consumption, had low HbA1c and a good antidiabetic effect, improved the histological structure of the islet.

Animal Model:	mice, Sprague Dawley rats, and beagle dogs[1]
Dosage:	1 mg/kg, 5 mg/kg and 10 mg/kg
Administration:	intravenous injection and oral administration
Result:	Displayed acceptable pharmacokinetic properties in different species.

REFERENCES

[1]. Yun Wu, et al. Discovery of IHMT-MST1-58 as a Novel, Potent, and Selective MST1 Inhibitor for the Treatment of Type 1/2 Diabetes. J Med Chem. 2022 Sep 8;65(17):11818-11839

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