HDAC6-IN-13

Cat. No.: HY-151261

CAS No.: 2837128-41-1

Molecular Formula: $C_{23}H_{22}N_4O$

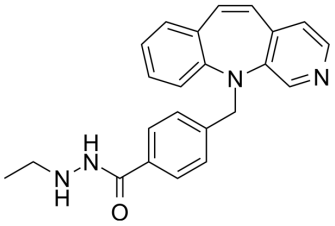
Molecular Weight: 370.45

Target: HDAC

Pathway: Cell Cycle/DNA Damage; Epigenetics

Storage:

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



SOLVENT & SOLUBILITY

In Vitro

DMSO : 125 mg/mL (337.43 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.6994 mL	13.4971 mL	26.9942 mL
	5 mM	0.5399 mL	2.6994 mL	5.3988 mL
	10 mM	0.2699 mL	1.3497 mL	2.6994 mL

Please refer to the solubility information to select the appropriate solvent.

BIOLOGICAL ACTIVITY

Description

HDAC6-IN-13 (Compound 35m) is a potent, highly selective, orally active HDAC6 inhibitor with an IC_{50} of 0.019 μM. HDAC6-IN-13 also inhibits HDAC1, HDAC2 and HDAC3 with IC_{50}s of 1.53, 2.06 and 1.03 μM, respectively. HDAC6-IN-13 shows significant BBB permeability and anti-inflammatory activity[1].

IC_{50} & Target

HDAC6	HDAC3	HDAC1	HDAC2
0.019 μM (IC_{50})	1.03 μM (IC_{50})	1.53 μM (IC_{50})	2.06 μM (IC_{50})

In Vitro

HDAC6-IN-13 (Compound 35m) (0.1-1 μM; 24 h) is highly selective toward HDAC6 versus class I HDACs[1].

HDAC6-IN-13 is a slow-on and slow-off tight-binding HDAC6 inhibitor, while exhibits fast-on properties for HDAC1, 2, and 3[1].

HDAC6-IN-13 (5-20 μM; 8 h) shows anti-inflammatory activity in vitro[1].

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

Western Blot Analysis[1]

Cell Line:	MV4−11 and J774A.1
Concentration:	0.1, 0.2, 0.5 and 1 μM

Incubation Time:	24 h
Result:	Concentration-related accumulation of acetylated tubulin (Ac-Tubulin) was observed, while upregulation of acetylated histone H3 (AcHH3) and acetylated histone H4 (AcHH4) was not apparent even at the concentration of 1 μM.

Western Blot Analysis[1]

Cell Line:	J774A.1 cells
Concentration:	5, 10 and 20 μM
Incubation Time:	8 h
Result:	Inhibited the cleavage of pro-caspase 1 to p20 in a dose-dependent manner, inhibited theinteraction between HDAC6 and dynein.

In Vivo

HDAC6-IN-13 (Compound 35m) (20 mg/kg; p.o. and i.p.; once) displays a remarkable inhibition in LPS-induced inflammation in mice[1].

HDAC6-IN-13 (20 mg/kg; p.o.; once) shows very high oral bioavailability (F% = 93.4%) and significant BBB permeability in mice[1].

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

Animal Model:	Male C57BL/6 WT mice, LPS-induced endotoxic shock model[1]
Dosage:	20 mg/kg
Administration:	PO and IP, immediately after the LPS injection
Result:	Significantly decreased the serum IL-1β levels in LPS-induced mice via both ip and po administration.

Animal Model:	Male CD-1 mice[1]
Dosage:	5 mg/kg or 20 mg/kg
Administration:	IV (5 mg/kg) or PO (20 mg/kg) (Pharmacokinetic Study)
Result:	Pharmacokinetics Characterization of HDAC6-IN-13 (Compound 35m) with iv and Oral Administration[a][1]

PK parameters	HDAC6-IN-13	HDAC6-IN-13
administered dose (mg/kg)	iv at 5 mg/kg	oral at 20 mg/kg
C_{max} (ng/mL)	4604 ± 551	5570 ± 551
$t_{1/2}$ (h)	7.95 ± 0.370	6.80 ± 0.145
AUC_{0-inf} (ng•h/mL)	2755 ± 395	10292 ± 1385

F%	n/a	93.4 ± 12.6

[a]HDAC6-IN-13 was administrated via iv and po (n = 3). The blood sample was collected at different time points after dosing, and the plasma concentration of HDAC6-IN-13 was determined via LC-MS/MS. The area under the plasma concentration versus time curve (AUC) was calculated using the linear trapezoidal method. The pharmacokinetic parameters were obtained using the noncompartmental method. Data are shown as mean ± SD.

REFERENCES

[1]. Yue K, et al. First-in-Class Hydrazide-Based HDAC6 Selective Inhibitor with Potent Oral Anti-Inflammatory Activity by Attenuating NLRP3 Inflammasome Activation. J Med Chem. 2022 Sep 8.

Caution: Product has not been fully validated for medical applications. For research use only.

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