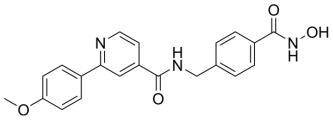
HDAC-IN-57

Cat. No.:	HY-149946
CAS No.:	2716217-79-5
Molecular Formula:	$C_{21}H_{19}N_3O_4$
Molecular Weight:	377.39
Target:	HDAC; Apoptosis; Histone Demethylase
Pathway:	Cell Cycle/DNA Damage; Epigenetics; Apoptosis
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description HDAC-IN-57 is an orally active inhibitor of histone deacetylases (HDAC), with IC_{50}s of 2.07 nM, 4.71 nM, 2.4 nM and 107 nM for HDAC1, HDAC2, HDAC6 HDAC8, respectively. HDAC-IN-57 can inhibits LSD1, with IC_{50} of 1.34 μM. HDAC-IN-57 induces apoptosis, and has anti-tumor activity[1].

IC_{50} & Target	HDAC1	HDAC2	HDAC6	HDAC8
	2.07 nM (IC_{50})	4.71 nM (IC_{50})	2.4 nM (IC_{50})	107 nM (IC_{50})

In Vitro

HDAC-IN-57 (Compound 5e) (1.0 μM, 2.5 μM, 5.0 μM☒48 hour) inhibits migration and invasion activity of MGC-803 and HCT-116 cells[1].

HDAC-IN-57 (1.0 μM, 2.5 μM, 5.0 μM☒48 hour) significantly inhibits the growth of solid tumor cell lines MGC-803, A549, and HCT-116, with IC_{50}s of 0.4 1.48 μM and 0.57 μM, respectively[1].

HDAC-IN-57 (1.0 μM. 2.5 μM, 5.0 μM; 48 hours) triggers apoptosis of MGC-803 and HCT -116 cells in a dose-dependent manner[1].

HDAC-IN-57 (1.0 μM. 2.5 μM, 5.0 μM; 48 hours) inhibits LSD1 and HDACs of MGC-803 and HCT -116 cells[1].

HDAC-IN-57 (1.0 μM. 2.5 μM, 5.0 μM; 48 hours) induces G2/M cycle arrest in MGC-803 and HCT-116 cells[1].

HDAC-IN-57 (Compound 5e) showes excellent metabolic stability in human liver (HLM) and rat liver microsomes (RLM), maintaining 86.1% and 87.4 respectively, of the parent compound after incubation for 1 h, with $T_{1/2}$ values over 120 min[1].

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

Western Blot Analysis[1]

Cell Line:	MGC-803 cells, HCT-116 cells
Concentration:	1.5 μM
Incubation Time:	48 hours
Result:	Inhibited cellular LSD1 and HDACs. Upregulated the expression of apoptotic markers, including cytochrome C, Bax, cleaved caspase-3/7/9, and cle PARP, while downregulating the expression of anti-apoptotic protein Bcl-2.

Apoptosis Analysis[1]

Cell Line:	MGC-803 cells, HCT-116 cells
Concentration:	1.0 μM, 2.5 μM, 5.0 μM
Incubation Time:	48 hours

Result:	Triggered MGC-803 and HCT116 cells apoptosis in a dose-dependent manner. Induced about 55.4% and 51.5% MGC-803 cell apoptosis at a concentration of 5 μM.

Cell Migration Assay [1]

Cell Line:	MGC-803 cells, HCT-116 cells
Concentration:	1.0 μM, 2.0 μM, 4 μM
Incubation Time:	48 hours
Result:	Reduced the number of migrated of MGC-803 and HCT-116 cells. Inhibited the migration and invasion of cancer

Cell Cycle Analysis[1]

Cell Line:	MGC-803 cells, HCT-116 cells
Concentration:	1.0 μM, 2.5 μM, 5.0 μM
Incubation Time:	48 hours
Result:	Induced G2/M cycle arrest in MGC-803 and HCT-116 cells.

In Vivo

HDAC-IN-57 (Compound 5e) (1 mg.kg for i.v., 10 mg/kg for p.o.) shows a $T_{1/2}$ of 0.37 h (i.v.) and 2.75 h (p.o.), and oral bioavailability (F%) of 10.6%[1].
HDAC-IN-57 (25 or 50 mg/kg, oral gavage once daily for 21 consecutive days) achieves a dose-dependent inhibition for tumor growth in an MGC-803 xenograft model with NOD-SCID mice[1].

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Animal Model:	MGC-803 xenograft model in NOD-SCID mice[1]
Dosage:	25 or 50 mg/ kg
Administration:	Oral gavage (p.o.);
Result:	Achieved a dose-dependent tumor growth inhibition (TGI) of 44.8% at 25 mg/kg and 71.5% at 50 mg/kg.

Animal Model:	Male SD rats (Pharmacokinetic assay)[1]
Dosage:	1 mg/kg; 10 mg/kg
Administration:	Intravenous injection (i.v.); Oral gavage (p.o.)
Result:	Pharmacokinetic parameters for HDAC-IN-57 (Compound 5e) in SD rats[1]

Route	Dose (mg/kg)	$T_{1/2}$ (h)	T_{max} (h)	CL (mL•min^{-1}/kg^{-1})	AUC_{0-t} (h•ng/mL)	$AUC_{0-\infty}$ (h•ng/mL)	C_{max} (ng/mL)	V_Z (L/kg)	F (%)
i.v.	1	0.37	/	1.61	644.1	645.8	1892.8	0.82	/
p.o.	10	2.75	0.25	/	685.2	766.2	716.4	52.2	10.6

REFERENCES

[1]. Duan Y, et al. Discovery of novel, potent, and orally bioavailable HDACs inhibitors with LSD1 inhibitory activity for the treatment of solid tumors. Eur J Med Che
Jun 5;254:115367.

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