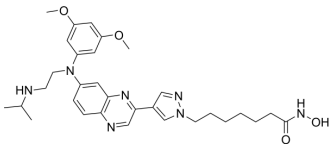
HDAC-IN-50

Cat. No.:	HY-152146
CAS No.:	2653339-26-3
Molecular Formula:	$C_{31}H_{41}N_7O_4$
Molecular Weight:	575.7
Target:	Apoptosis; FGFR; HDAC
Pathway:	Apoptosis; Protein Tyrosine Kinase/RTK; Cell Cycle/DNA Damage; Epigenetics
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

HDAC-IN-50 is a potent and orally active FGFR and HDAC dual inhibitor with IC_{50} values of 0.18, 1.2, 0.46, 1.4, 1.3, 1.6, 2.6, 13 nM for FGFR1, FGFR2, FGFR3, FGFR4, HDAC1, HDAC2, HDAC6, HDAC8, respectively. HDAC-IN-50 induces Apoptosis and cell cycle arrest at G0/G1 phase. HDAC-IN-50 decreases the expression of pFGFR1, pERK, pSTAT3. HDAC-IN-50 shows anti-tumor activity[1].

IC_{50} & Target

FGFR1 0.18 nM (IC_{50})	FGFR2 1.2 nM (IC_{50})	FGFR3 0.46 nM (IC_{50})	FGFR4 1.4 nM (IC_{50})
HDAC1 1.3 nM (IC_{50})	HDAC2 1.6 nM (IC_{50})	HDAC6 2.6 nM (IC_{50})	HDAC8 13 nM (IC_{50})

In Vitro

HDAC-IN-50 (compound 10e) (0.1, 1, 10, 100 nM; 12-84 h) induces apoptosis and cell cycle arrest at G0/G1 phase in a time and dose-dependent manner[1].

HDAC-IN-50 (0, 1.25, 2.5, 5 μM for HCT116 cells, 0, 1, 10, 100 nM for SNU-16 cells; 36 h) decreases the expression of pFGFR1, pERK, pSTAT3 in a dose-dependent manner[1].

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

Cell Proliferation Assay[1]

Cell Line:	HCT116, SNU-16, KATO III, A2780, K562, Jurkat cells
Concentration:	0-30 μM
Incubation Time:	72 h
Result:	Showed antiproliferative activities with IC_{50}s of 0.82, 0.0007, 0.0008, 0.04, 2.46, 15.14 μM for HCT116, SNU-16, KATO III, A2780, K562, Jurkat cells, respectively.

Cell Cycle Analysis[1]

Cell Line:	SNU-16 cells
Concentration:	0.1, 1, 10, 100 nM
Incubation Time:	12, 24, 36 h

Result:	Induced cell cycle arrest at G0/G1 phase in a time and dose-dependent manner.

Apoptosis Analysis[1]

Cell Line:	SNU-16 cells
Concentration:	0.1, 1, 10, 100 nM
Incubation Time:	36, 48, 60, 72, 84 h
Result:	Induced apoptosis with the apoptotic rate increased 30.8% and 49.6% at 10, 100 nM, respectively.

Western Blot Analysis[1]

Cell Line:	HCT116, SNU-16 cells
Concentration:	0, 1.25, 2.5, 5 μM for HCT116 cells, 0, 1, 10, 100 nM for SNU-16 cells
Incubation Time:	36 h
Result:	Reduced the expression of pFGFR1, pERK, pSTAT3 in a dose-dependent manner.

In Vivo

HDAC-IN-50 (15, 30 mg/kg; p.o.; daily for 18 days) shows anti-tumor activity in mouse[1].
Pharmacokinetic Parameters of HDAC-IN-50 in female Sprague–Dawley (SD) rats[1].

dose (mg/kg)	administration route	$T_{1/2}$ (h)	T_{max} (h)	C_{max} (ng/mL)	$AUC_{0-\infty}$ (h·ng/mL)	CL (mL/min/kg)	V_{ss} (mL/kg)	F %
2	IV	0.98± 0.12	0.08	1116.63 ± 320.45	424.88 ± 89.56	80.64 ± 15.59	2788.87 ± 765.11	
5	IP	1.83 ± 0.06	2	101.57 ± 23.05	491.25 ± 84.18			43.83
30	PO	0.77 ± 0.04	4	442.53 ± 46.33	1557.12 ± 355.61			24.83

Female Sprague-Dawley (SD) rats, 5 mg/kg iv; 5 mg/kg ip; 30 mg/kg p.o.[1]
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	BALB/c nude mice (HCT116 xenograft model)[1]
Dosage:	15, 30 mg/kg
Administration:	P.o.; daily for 18 days
Result:	Inhibited the tumor growth and downregulated the expression of pSTAT3, pFGFR1, increased the expression of Ac-H3.

REFERENCES

[1]. Wan G, et al. Design and Synthesis of Fibroblast Growth Factor Receptor (FGFR) and Histone Deacetylase (HDAC) Dual Inhibitors for the Treatment of Cancer. J Med Chem. 2022 Dec 22;65(24):16541-16569.

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