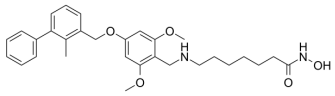
HDAC6-IN-4

Cat. No.:	HY-144395
CAS No.:	2709103-20-6
Molecular Formula:	$C_{30}H_{38}N_2O_5$
Molecular Weight:	506.63
Target:	HDAC; Apoptosis
Pathway:	Cell Cycle/DNA Damage; Epigenetics; Apoptosis
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

HDAC6-IN-4 (C10) is a potent, orally active and highly selective HDAC6 inhibitor with an IC_{50} value of 23 nM. HDAC6-IN-4 induces cancer cells apoptosis and shows significant antitumor efficacy, without obvious toxicity[1].

IC_{50} & Target

HDAC6 23 nM (IC_{50})	HDAC3 46 nM (IC_{50})	HDAC2 172 nM (IC_{50})	HDAC8 2175 nM (IC_{50})
HDAC1 3604 nM (IC_{50})			

In Vitro

HDAC6-IN-4 (C10) (0-50 μM, 72 h) shows strong antiproliferative activity against different cancer cells with low cytotoxicity[1].
HDAC6-IN-4 (0-6 μM, 24 h) exhibits significant selectivity for HDAC6 over HDAC1[1].
HDAC6-IN-4 inhibits migration activity in a time-dependent and dose-dependent way in B16 and CT26 cells[1].
HDAC6-IN-4 (0-8 μM, 24 h) induces B16 cell apoptosis in a dose-dependent manner[1].
HDAC6-IN-4 exhibits significant plasma stability in humans (97% retention after 6 h), and exhibits significant metabolic stability in human (half-life of 101.91 min) and mouse liver (half-life of 67.94 min) microsomes[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Proliferation Assay[1]

Cell Line:	B16, HepG2, A549, and CT26 cells
Concentration:	0-50 μM
Incubation Time:	72 h
Result:	Showed antiproliferative activity with IC_{50} values of 1.52, 2.36, 5.77, and 2.09 μM against B16, HepG2, A549, and CT26 cells, respectively.

Western Blot Analysis[1]

Cell Line:	B16 and CT26 cancer cells
Concentration:	2, 4, and 6 μM
Incubation Time:	2, 4, 8, 12, and 24 h

Result:	Dramatically increased the level of Ac-Tub (acetyl-α-tubulin) in a dose-dependent and time-dependent manner. Had almost no effect on the content of Ac-H3 (acetyl-H3).

Apoptosis Analysis[1]

Cell Line:	B16 cells
Concentration:	4, 6, and 8 μM
Incubation Time:	24 h
Result:	Caused moderate to potent induction of apoptosis in the B16 cell line in a dose-dependent manner. Upregulated the expression of apoptotic protein cleaved PARP.

In Vivo

HDAC6-IN-4 (C10) (0-100 mg/kg; i.g.; once daily for 21 days) shows excellent antitumor activity and significantly promoted T cell response in a dose-dependent manner, with no obvious toxicity[1].

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

Animal Model:	Five-week-old C57BL/6 mice (immune-related CT26 xenograft model)[1].
Dosage:	50 and 100 mg/kg
Administration:	Oral gavage, once daily for 21 days
Result:	Resulted in a substantial tumor growth and tumor tissue size inhibition in a dose-dependent way. Showed significantly high antitumor activity (TGI = 75%) at 100 mg/kg. Raised the plasma IFN-g level and the numbers of CD^+ and $CD3^+CD^+$ (activated cytotoxic T) cells. Decreased $CD4^+CD25^+CD127^{low/-}$ T regulatory cells. Showed no obvious toxicity.

REFERENCES

[1]. Xi Xu, et al. Novel biphenyl-based scaffold as potent and selective histone deacetylase 6 (HDAC6) inhibitors: Identification, development and pharmacological evaluation. Eur J Med Chem. 2022 Apr 5;233:114228.

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