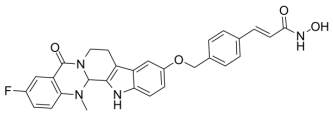
HDAC/Top-IN-1

Cat. No.:	HY-144654
CAS No.:	2411379-14-9
Molecular Formula:	$C_{29}H_{25}FN_4O_4$
Molecular Weight:	512.53
Target:	HDAC; Topoisomerase
Pathway:	Cell Cycle/DNA Damage; Epigenetics
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

HDAC/Top-IN-1 is an orally active and pan HDAC/Top dual inhibitor with IC_{50}s of 0.036 μM, 0.14 μM, 0.059 μM, 0.089 μM and 9.8 μM for HDAC1, HDAC2, HDAC3, HDAC6 and HDAC8. HDAC/Top-IN-1 efficiently induces apoptosis with S cell-cycle arrest in HEL cells. HDAC/Top-IN-1 has exhibits excellent in vivo antitumor efficacy[1].

IC_{50} & Target

HDAC1	HDAC2	HDAC3	HDAC6
34 nM (IC_{50})	140 nM (IC_{50})	59 nM (IC_{50})	89 nM (IC_{50})

HDAC8
9.8 μM (IC_{50})

In Vitro

HDAC/Top-IN-1 (compound 16j) (0-2 μM; 48 hours) exhibits remarkable inhibitory activities against the tested cell lines[1].
HDAC/Top-IN-1 (20 and 100 nM; 24 hours) dramatically increases acetyl-H3 and acetyl-H4 levels in HEL cells[1].
HDAC/Top-IN-1 (0.1 and 0.5 μM; 48 hours) effectively induces HEL cell apoptosis in a dose-dependent manner[1].
HDAC/Top-IN-1 (0.02-0.5 μM; 48 hours) arrests HEL cells at the S phase[1].

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

Cell Proliferation Assay

Cell Line:	MCF-7, A549, HCT116, HepG-2, K562 and HEL[1]
Concentration:	0-2 μM
Incubation Time:	48 hours
Result:	Exhibited remarkable inhibitory activities against the tested cell lines, and IC_{50}s of 0.68, 0.21, 0.26, 0.35 and 0.029 μM in MCF-7, A549, HCT116, HepG-2, K562 and HEL, respectively.

Western Blot Analysis

Cell Line:	HEL[1]
Concentration:	20 and 100 nM
Incubation Time:	24 hours
Result:	Dramatically increased in acetyl-H3 and acetyl-H4 levels.

Apoptosis Analysis

Cell Line:	HEL[1]
Concentration:	0.1 and 0.5 μM
Incubation Time:	48 hours
Result:	Led to 56.02% and 76.45% apoptotic cell death at concentration of 0.1 and 0.5 μM, respectively

Cell Cycle Analysis

Cell Line:	HEL[1]
Concentration:	0.02, 0.1 and 0.5 μM
Incubation Time:	48 hours
Result:	The ratios in the S phase were changed dramatically 9.8%, 15.4%, and 25.8% at 0.02, 0.1 and 0.5 μM, respectively.

In Vivo

HDAC/Top-IN-1 exhibits good metabolic properties with a half-life ($T_{1/2}$) of 31.49 min, and the clearance is 173.32 mL/min/mg[1].
HDAC/Top-IN-1 (5 and 10 mg/kg; PO; daily, for 14 days) exhibits potent oral antitumor activity[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Female BALB/C nude mice (5-6 weeks, 18-20 g; injected with human K562 cells)[1]
Dosage:	5 and 10 mg/kg
Administration:	PO; daily, for 14 days
Result:	Exhibited potent oral antitumor activity at 5 mg/kg with a TGI value of 41.4% and a T/C value of 54.3%, and achieved better tumor growth inhibition with a TGI of 68.5% and a T/C of 25.5%.

REFERENCES

[1]. Wu S, Huang Y, Wang T, et al. Evodiamine-Inspired Topoisomerase-Histone Deacetylase Dual Inhibitors: Novel Orally Active Antitumor Agents for Leukemia Therapy. J Med Chem. 2022;65(6):4818-4831.

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