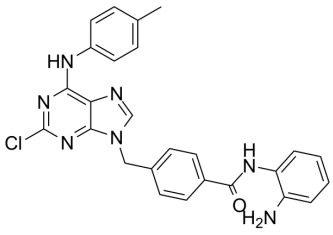
HDAC1/2 and CDK2-IN-1

Cat. No.:	HY-143497
CAS No.:	2418559-01-8
Molecular Formula:	$C_{26}H_{22}ClN_7O$
Molecular Weight:	483.95
Target:	HDAC; CDK; 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

HDAC1/2 and CDK2-IN-1 (compound 14d) is a potent HDAC1, HDAC2 and CDK2 dual inhibitor, with IC_{50} values of 70.7, 23.1 and 0.80 μM, respectively. HDAC1/2 and CDK2-IN-1 can block the cell cycle and induce apoptosis. HDAC1/2 and CDK2-IN-1 exhibits desirable in vivo antitumor activity[1].

IC_{50} & Target

HDAC1	HDAC2	CDK2
70.7 nM (IC_{50})	23.1 nM (IC_{50})	0.80 nM (IC_{50})

In Vitro

HDAC1/2 and CDK2-IN-1 (compound 14d) shows excellent antiproliferative activities against H460, A375, HepG2, HCT116 and Hela cells with IC_{50} values of 1.59, 0.47, 0.86, 0.58 and 1.05 μM, respectively[1].
HDAC1/2 and CDK2-IN-1 (0.5 μM, 48 h) significantly inhibits the migration of H460 and A375 cells[1].
HDAC1/2 and CDK2-IN-1 (0-2 μM, 24 h) significantly blocks the cell cycle in the G2/M phase[1].
HDAC1/2 and CDK2-IN-1 (0-2 μM, 48 h) promotes cancer cell apoptosis in a dose-dependent manner[1].
HDAC1/2 and CDK2-IN-1 (1 μM, 12 h) inhibits CDK2 and HDAC activity, causing cancer cell death[1].
HDAC1/2 and CDK2-IN-1 (1 μM, 24 h) strongly increases ROS levels in A375 cells, causes cancer cell death by improving intracellular ROS levels[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Cycle Analysis

Cell Line:	A375, HCT116, H460 and Hela cells[1]
Concentration:	0, 0.5, 1, 2 μM
Incubation Time:	24 h
Result:	Significantly blocked the cell cycle, induced a loss of G0/G1 phase cells and an increase of G2/M phase cells, led to an apparent accumulation of cells in G2/M phase at 0.5 μM (A375, the percentage from 13.70 to 57.03%; HCT116, from 27.46 to 76.99%; Hela, from 7.89% to 51.85%).

Apoptosis Analysis

Cell Line:	A375, HCT116, H460 and Hela cell lines[1]
Concentration:	0, 0.5, 1, 2 μM

Incubation Time:	48 h
Result:	Promoted cancer cell apoptosis in a dose-dependent manner, with the apoptosis rates of 91.99% (A375), 89.60% (HCT116), 59.10% (H460), and 22.36% (Hela) respectively at the concentration of 2 μM.

Immunofluorescence

Cell Line:	A375 cells[1]
Concentration:	1 μM
Incubation Time:	12 h
Result:	Significantly inhibited CDK2 and increased the acetylation level of histone H3, inhibited CDK2 and HDAC activity, causing cancer cell death.

In Vivo

HDAC1/2 and CDK2-IN-1 (BALB/c nude mice, 0-100 mg/kg, IP, once daily for 21 days) significantly inhibits the tumor growth [1].

HDAC1/2 and CDK2-IN-1 (compound 14d) (ICR mice; 4 mg/kg, IV; 20 mg/kg, IP) exhibits desirable pharmacokinetic properties [1].

Pharmacokinetic Parameters of HDAC1/2 and CDK2-IN-1 in male ICR mice[1].

Dose (mg/kg)	4	20
Administration	IV	IP
$T_{1/2}$ (h)	1.48	2.84
T_{max} (h)		2
C_{max} (ng/mL)		1360
AUC_{0-t} (ng/mL*h)	2850	7240
MRT_{0-t} (h)	0.563	4.54
CL (mL/(min/kg))	23.3	
F (%)		50.8

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Animal Model:	Male ICR mice (n = 9)[1]
Dosage:	4 mg/kg (IV), 20 mg/kg (IP)
Administration:	IV, IP, once (Pharmacokinetic Analysis)
Result:	Exhibited desirable pharmacokinetic properties.

Animal Model:	BALB/c nude mice (5-6 weeks, HCT116 xenograft model)[1]
Dosage:	0, 25, 50 and 100 mg/kg
Administration:	IP, once daily for 21 days
Result:	Significantly inhibited the tumor growth, the tumor growth inhibitions were 28%, 40% and 44% at doses of 25, 50 and 100 mg/kg, respectively.

REFERENCES

[1]. Yun F, Cheng C, Ullah S, Yuan Q. Design, synthesis and biological evaluation of novel histone deacetylase1/2 (HDAC1/2) and cyclin-dependent Kinase2 (CDK2) dual inhibitors against malignant cancer. Eur J Med Chem. 2020;198:112322.

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