CDK/HDAC-IN-2

Cat. No.: HY-146276

CAS No.: 2580938-58-3

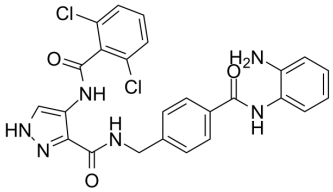
Molecular Formula: $C_{25}H_{20}Cl_2N_6O_3$

Molecular Weight: 523.37

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

CDK/HDAC-IN-2 is a potent HDAC/CDK dual inhibitor with IC_{50} of 6.4, 0.25, 45, >1000, 8.63, 0.30, >1000 nM for HDAC1, HDAC2, HDAC3, HDAC6,8, CDK1, CDK2, CDK4,6,7, respectively. CDK/HDAC-IN-2 shows excellent antiproliferative activities. CDK/HDAC-IN-2 induces apoptosis and cell cycle arrest at G2/M phase. CDK/HDAC-IN-2 shows potent antitumor efficacy[1].

IC_{50} & Target

HDAC1 6.4 nM (IC_{50})	HDAC2 0.25 nM (IC_{50})	HDAC3 45 nM (IC_{50})	HDAC6 >1000 nM (IC_{50})
HDAC8 >1000 nM (IC_{50})	CDK1 8.63 nM (IC_{50})	CDK2 0.30 μM (IC_{50})	CDK4 >1000 nM (IC_{50})
CDK6 >1000 nM (IC_{50})	CDK7 >1000 nM (IC_{50})		

In Vitro

CDK/HDAC-IN-2 (compound 7c) shows antiproliferative activity with IC_{50}s of 0.71, 1.20, 1.83, 4.19, 7.76, 4.47 μM for HCT116, A375, Hela, H460, SMMC7721, NIH 3T3 cells, respectively[1].

CDK/HDAC-IN-2 (24 h) shows anti-migration ability in A375 and H460 cells[1].

CDK/HDAC-IN-2 (0.5, 1, 2 μM) induces apoptosis and cell cycle arrest at G2/M phase[1].

CDK/HDAC-IN-2 accelerates intracellular ROS accumulation, leading to cancer cell death[1].

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

Cell Cycle Analysis[1]

Cell Line:	A375, HCT116, H460, Hela cells
Concentration:	0.5, 1, 2 μM
Incubation Time:	24 h
Result:	Induced cell cycle arrest at G2/M phase.

Apoptosis Analysis[1]

Cell Line:	A375, HCT116, H460, Hela cells
Concentration:	0.5, 1, 2 μM

Incubation Time:	48 h
Result:	Induced cell apoptosis with the apoptosis rates of A375, HCT116 cells of 97.22%, 60.6%, respectively.

In Vivo

CDK/HDAC-IN-2 (12.5, 25 mg/kg; IP; once daily for 21 days) shows antitumor efficacy in the HCT116 xenograft model (TGI= 51.0%)[1].

Pharmacokinetic Parameters of CDK/HDAC-IN-2 in ICR male mice[1].

compound	7c
Dose (mg/kg)	20
administration	i.p.
$t_{1/2}$ (h)	2.61
T_{max} (h)	2.00
C_{max} (h)	7570
$AUC_{0-\infty}$ (ng h/mL)	30700
$MRT_{0-\infty}$ (ng h/mL)	3.31
F (%)	63.6

ICR male mice; 20 mg/kg, i.p.[1].

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

Animal Model:	ICR male mice[1]
Dosage:	20 mg/kg
Administration:	IP
Result:	Showed good Pharmacokinetic parameters with bioavailability of F= 63.6%.

Animal Model:	5-6 weeks, BALB/c female mice (HCT116 xenograft nude mice models)[1]
Dosage:	12.5, 25 mg/kg
Administration:	IP, once daily for 21 days
Result:	Effectively inhibited the growth of HCT116 xenograft tumors tumor growth inhibitions (TGI) at 12.5 and 25 mg/kg of 37.0% and 51.0%, respectively.

REFERENCES

[1]. Cheng C, et al. Discovery of novel cyclin-dependent kinase (CDK) and histone deacetylase (HDAC) dual inhibitors with potent in vitro and in vivo anticancer activity. Eur J Med Chem. 2020 Mar 1;189:112073.

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