CDK8-IN-11 hydrochloride

Cat. No.: HY-151463A

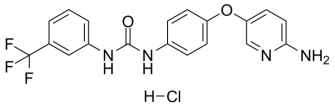
Molecular Formula: $C_{19}H_{16}ClF_3N_4O_2$

Molecular Weight: 424.8

Target: CDK; β-catenin

Pathway: Cell Cycle/DNA Damage; Stem Cell/Wnt

Storage: Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

CDK8-IN-11 hydrochloride is a potent and selective CDK8 inhibitor with an IC_{50} value of 46 nM. CDK8-IN-11 hydrochloride inhibits WNT/β-catenin signaling pathway. CDK8-IN-11 hydrochloride can be used in the research of colon cancer[1].

In Vitro

CDK8-IN-11 (compound 29, 200 nM) hydrochloride shows inhibitory effects against CDK8 by 73.6% [1].

CDK8-IN-11 (0-50 μM, 48 h) hydrochloride inhibits cell proliferation in HCT-116, HHT-29, SW480, CT-26, GES-1 cells[1].

CDK8-IN-11 (0-4 μM, 48 h) hydrochloride inhibits the phosphorylation of STAT1 at Ser727 mediated by CDK8 in HCT-116 cells [1].

CDK8-IN-11 (0-4 μM, 24 h) hydrochloride suppresses canonical WNT/β-catenin signaling pathways and deregulates β-catenin-mediated transcription in HCT-116 cells[1].

CDK8-IN-11 (0.5-2 μM, 48 h) hydrochloride increases the number of cells in the G1 phase in HCT-116 cells[1].

CDK8-IN-11 (0-4 μM) hydrochloride reverses Sorafenib (HY-10201) resistance of HCT-116 cells[1].

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

Cell Proliferation Assay[1]

Cell Line:	HCT-116, HHT-29, SW480, CT-26, GES-1 cells
Concentration:	0.08, 0.4, 2, 10, and 50 μM
Incubation Time:	48 h
Result:	Inhibited cell proliferation with IC_{50} values of 1.2, 0.7, 2.4, 5.5, 62.7 nM respectively.

Western Blot Analysis[1]

Cell Line:	HCT-116 cell
Concentration:	0, 1, 2, 4 μM
Incubation Time:	48 h
Result:	Inhibited the phosphorylation of STAT1 at Ser727 without affecting the JAK-regulated phosphorylation at Tyr701.

Cell Cycle Analysis[1]

Cell Line:	HCT-116 cell
Concentration:	0.5-2 μM
Incubation Time:	48 h
Result:	Increased the number of cells in the G1 phase with an obvious decreased percentage of cells in the G2/M and S phase in HCT-116 cells.

In Vivo

CDK8-IN-11 (compound 29, 10 and 40 mg/kg, p.o.) hydrochloride inhibits tumor growth in CT-26 xenograft mice[1].
CDK8-IN-11 (1000 mg/kg, oral gavage, ICR mice) hydrochloride shows no obvious abnormal behavior within 7 days[1].
CDK8-IN-11 (10 mg/kg, p.o.; 2 mg/kg, i.v., rats) hydrochloride shows moderate permeability with an apparent permeability coefficient value of 1.8×10^{-6} cm/s[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	CT-26 xenograft mice[1]
Dosage:	10 and 40 mg/kg
Administration:	Oral adminstration (p.o.)
Result:	Reduced the tumor volume, reduced β-catenin and c-Myc level in tumor.

Animal Model:	Reduced the tumor volume, reduced β-catenin and c-Myc level in tumor.
Dosage:	10 mg/kg (p.o.), 2 mg/kg (i.v.)
Administration:	Oral adminstration (p.o.) or intravenous injection (i.v.)
Result:	Pharmacokinetic profile of CDK8-IN-11 (compound 29).

dose (mg/kg)	$T_{1/2}$ (h)	T_{max} (h)	C_{max} (ng/mL)	F (%)
10 (p.o.)	1.1	0.8	453	31.7
2 (i.v.)	0.5		318	

REFERENCES

[1]. Yao Yao Yan, et al. Design and Synthesis of a 2-Amino-pyridine Derivative as a Potent CDK8 Inhibitor for Anti-colorectal Cancer Therapy. J Med Chem. 2022 Sep 20.

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