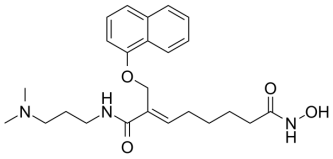
Ivaltinostat

Cat. No.:	HY-16138
CAS No.:	936221-33-9
Molecular Formula:	$C_{24}H_{33}N_3O_4$
Molecular Weight:	427.54
Target:	HDAC; MDM-2/p53; 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

Ivaltinostat (CG-200745) is an orally active, potent pan-HDAC inhibitor which has the hydroxamic acid moiety to bind zinc at the bottom of catalytic pocket. Ivaltinostat inhibits deacetylation of histone H3 and tubulin. Ivaltinostat induces the accumulation of p53, promotes p53-dependent transactivation, and enhances the expression of MDM2 and p21 (Waf1/Cip1) proteins. Ivaltinostat enhances the sensitivity of Gemcitabine-resistant cells to Gemcitabine (HY-16138) and 5-Fluorouracil (5-FU; HY-90006). Ivaltinostat induces apoptosis and has anti-tumour effects[1][2][3][4].

IC_{50} & Target

HDAC

In Vitro

Ivaltinostat (CG-200745; 0.01-100 μM; 48 hours) inhibits growth of prostate cancer cells (LNCaP, DU145 and PC3 cells).
Ivaltinostat (1, 10 μM; 24, 48 hours) increases sub-G1 population, and activates caspase-9, -3 and -8[2].
Ivaltinostat (0.001-100 μM; for 72 hours) inhibits proliferation of cholangiocarcinoma cells (IC50s of 0.63, 0.93, and 1.80 μM for SNU-1196, SNU-1196/GR, SNU-308 cells, respectively)[3].
Ivaltinostat (0-10 μM; 48 hours) reduces the Calu6 cells proliferation to 40% of untreated cells[4].
Ivaltinostat (3 μM; 1-24 hours) significantly increases Calu6 cells proportion in G2/M phase (69%)[4].
Ivaltinostat (0-10 μM; 1-24 hours) treatment with low concentration significantly increases the acetylation of histone H3 and H4 in Calu6 cells at various sites in a time-dependent manner up to 24 hours after treatment[4].

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

Cell Proliferation Assay[4]

Cell Line:	Calu6 cells
Concentration:	0-10 μM
Incubation Time:	48 hours
Result:	Reduced the cell proliferation to 40% of untreated cells.

Cell Cycle Analysis[4]

Cell Line:	Calu6 cells
Concentration:	3 μM
Incubation Time:	1, 8, 12, 24 hours

Result:	Increased significantly cell proportion in G2/M phase (69%).

Western Blot Analysis[4]

Cell Line:	Calu6 cells
Concentration:	0-10 μM
Incubation Time:	1, 4, 8, 12, 24 hours
Result:	Increased the acetylation of histone H3 and H4 at various sites in a time-dependent manner.

In Vivo

Ivaltinostat (CG-200745; p.o.; 30 mg/kg/day; for 7 days) attenuates oxidative stress, inflammatory cytokines, and adhesion molecules in UUO kidneys[5].

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

Animal Model:	Male 8-week-old C57BL/6 J mice weighing 20~22 g of unilateral ureteral obstruction (UUO) [5]
Dosage:	30 mg/kg
Administration:	PO; daily; for 7 days
Result:	Attenuated oxidative stress, inflammatory cytokines and adhesion molecules in UUO kidneys.

REFERENCES

[1]. Oh ET, et al. Novel histone deacetylase inhibitor CG200745 induces clonogenic cell death by modulating acetylation of p53 in cancer cells. Invest New Drugs. 2012 Apr;30(2):435-42.

[2]. Hwang JJ, et al. A novel histone deacetylase inhibitor, CG200745, potentiates anticancer effect of docetaxel in prostate cancer via decreasing Mcl-1 and Bcl-XL. Invest New Drugs. 2012 Aug;30(4):1434-42.

[3]. Chun SM, et al. Epigenetic modulation with HDAC inhibitor CG200745 induces anti-proliferation in non-small cell lung cancer cells. PLoS One. 2015 Mar 17;10(3):e0119379.

[4]. Choi HS, et al. Histone deacetylase inhibitor, CG200745 attenuates renal fibrosis in obstructive kidney disease. Sci Rep. 2018 Aug 1;8(1):11546.

[5]. Dawoon E Jung, et al. CG200745, an HDAC inhibitor, induces anti-tumour effects in cholangiocarcinoma cell lines via miRNAs targeting the Hippo pathway. Sci Rep. 2017 Sep 7;7(1):10921.

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