Ivaltinostat formic

Cat. No.: HY-16138A

Molecular Formula: $C_{25}H_{35}N_3O_6$

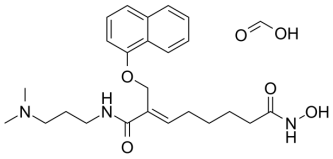
Molecular Weight: 473.56

Target: HDAC; Apoptosis; MDM-2/p53

Pathway: Cell Cycle/DNA Damage; Epigenetics; Apoptosis

Storage: 4°C, sealed storage, away from moisture

* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (105.58 mM; Need ultrasonic)

H_2O : 50 mg/mL (105.58 mM; Need ultrasonic)

Preparing Stock Solutions

Concentration \ Solvent Mass	1 mg	5 mg	10 mg
1 mM	2.1117 mL	10.5583 mL	21.1166 mL
5 mM	0.4223 mL	2.1117 mL	4.2233 mL
10 mM	0.2112 mL	1.0558 mL	2.1117 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: PBS
   Solubility: 50 mg/mL (105.58 mM); Clear solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (5.28 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.28 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.28 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

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

IC_{50} & Target	HDAC

In Vitro

Ivaltinostat (CG-200745; 0.01-100 μM; 48 hours) formic inhibits growth of prostate cancer cells (LNCaP, DU145 and PC3 cells).
Ivaltinostat (1, 10 μM; 24, 48 hours) formic 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 (IC_{50}s 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) formic reduces the Calu6 cells proliferation to 40% of untreated cells[4].
Ivaltinostat (3 μM; 1-24 hours) formic significantly increases Calu6 cells proportion in G2/M phase (69%)[4].
Ivaltinostat (0-10 μM; 1-24 hours) formic 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:	3 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) formic 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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