Dacinostat

Cat. No.: HY-13606

CAS No.: 404951-53-7

Molecular Formula: $C_{22}H_{25}N_3O_3$

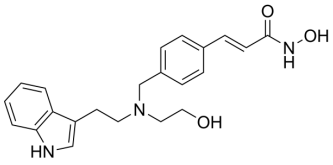
Molecular Weight: 379.45

Target: HDAC; Autophagy

Pathway: Cell Cycle/DNA Damage; Epigenetics; Autophagy

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 43 mg/mL (113.32 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.6354 mL	13.1770 mL	26.3539 mL
5 mM	0.5271 mL	2.6354 mL	5.2708 mL
10 mM	0.2635 mL	1.3177 mL	2.6354 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (6.59 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.59 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.59 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Dacinostat is a potent HDAC inhibitor, with an IC_{50} of 32 nM; Dacinostat also inhibits HDAC1 with an IC_{50} of 9 nM, and used in cancer research.

IC_{50} & Target

HDAC1	HDAC
9 nM (IC_{50})	32 nM (IC_{50})

In Vitro	Dacinostat (NVP-LAQ824) activates p21 promoter, with AC_{50} of 0.30 μM. NVP-LAQ824 inhibits tumor cell (H1299, HCT116) growth, with IC_{50}s of 150 and 10 nM, respectively. NVP-LAQ824 also shows inhibitory activities against two prostate cancer cell lines (DU145 and PC3) and a breast cancer line (MDA435), with IC_{50}s of 18, 23, 39 nM, respectively. Continuous exposure of NVP-LAQ824 for 72 h produces LD90s of 0.09 M in HCT116 cells and 0.47 M in A549 cells. NVP-LAQ824 treatment of NDHF cells causes the expected G1-S growth arrest in addition to a significant reduction of cells in S-phase and accumulation of cells at the G2-M checkpoint. NVP-LAQ824 induces apoptotic death in human tumor cells. NPV-LAQ824 increases acetylation of histones H3 and H4[1]. Dacinostat inhibits HDAC1 with an IC_{50} of 9 nM[2]. Dacinostat (10 and 20 nM) suppresses proliferation of AML fusion protein-expressing 32D cells. Dacinostat impairs short-term engraftment potential of leukemic stem cells. Dacinostat exhausts in vitro self-renewal potential of murine AML1/ETO- and PLZF/RARα-positive HSC[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	NVP-LAQ824 produces a dose-dependent inhibition of tumor growth, and at 100 mg/kg, its antitumor effect is similar to that of 5-Fluorouracil[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [2]	The HDAC enzymatic assay measures compound activity in inhibiting purified HDAC isoforms. HDACs 1, 3, and 6 are immunopurified from 293 cells stably expressing the FLAG-tagged HDAC isoform, whereas HDACs 2, 4, 5, 7, 8, 9, 10, and 11 are purified from the baculovirus expression system. HDAC activity is measured in a fluorescent assay in which deacetylation of the substrate, bis-Boc-(Ac)Lys-rhodamine 110, generates a fluorophore that can be detected on a fluorometric plate reader[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [2]	Cells are plated at 5000−10000 cells per well in 96-well plates and treated with eight serial compound dilutions. Cell viability following 72 h of compound treatment is measured using the CellTiter-Glo or MTS assay. XLfit 4 is used for plotting of the growth curves and calculation of IC_{50} values[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	The studies are performed on-site, using outbred athymic (nu/nu) female mice. Mice are anesthetized with Metofane, and a cell suspension (100 μL) containing 1×10^6 HCT116 cells is injected s.c. into the right axillary (lateral) region of each animal. Tumors are allowed to reach the volume of approximately 100-400 mm^3. At this point, mice bearing tumors with acceptable morphology (non-necrotic) and of similar size range are selected and distributed into groups of six for the studies. NVP-LAQ824 is dissolved in DMSO to create a stock solution, which is further diluted just before dosing with D5W to a final DMSO concentration of 10%. Tumor-bearing mice are treated with the compound by i.v. injection into the tail vein. NVP-LAQ824 is dosed once daily, 5 days/week, for a total of 15 doses. 5-Fluorouracil is administered at 100 mg/kg in 0.9% saline 1 day/week for a total of three doses. The control groups are treated with the vehicle. Tumors are collected from the animals at the indicated time points[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Proc Natl Acad Sci U S A. 2019 Feb 19;116(8):2961-2966.
- BBA-Mol Basis Dis. 2021, 166169.
- Exp Hematol Oncol. 2019 Nov 15;8:30.

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REFERENCES

[1]. Atadja P, et al. Selective growth inhibition of tumor cells by a novel histone deacetylase inhibitor, NVP-LAQ824. Cancer Res. 2004 Jan 15;64(2):689-95.

[2]. Cho YS, et al. Conformational refinement of hydroxamate-based histone deacetylase inhibitors and exploration of 3-piperidin-3-ylindole analogues of dacinostat (LAQ824). J Med Chem. 2010 Apr 8;53(7):2952-63.

[3]. Romanski A, et al. Deacetylase inhibitors modulate proliferation and self-renewal properties of leukemic stem and progenitor cells. Cell Cycle. 2012 Sep 1;11(17):3219-26.

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