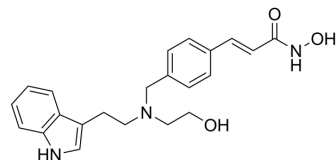


Dacinostat

Cat. No.:	HY-13606		
CAS No.:	404951-53-7		
Molecular Formula:	C ₂₂ H ₂₅ N ₃ O 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	6 months
		-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 43 mg/mL (113.32 mM)
 * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent Concentration	Mass		
		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

- 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
- 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
- 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 IC₅₀ of 32 nM; Dacinostat also inhibits HDAC1 with an IC₅₀ of 9 nM, and used in cancer research.

IC₅₀ & Target

HDAC1 9 nM (IC ₅₀)	HDAC 32 nM (IC ₅₀)
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In Vitro	<p>Dacinostat (NVP-LAQ824) activates p21 promoter, with AC₅₀ of 0.30 μM. NVP-LAQ824 inhibits tumor cell (H1299, HCT116) growth, with IC₅₀s 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 IC₅₀s 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 IC₅₀ 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.</p>
In Vivo	<p>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.</p>

PROTOCOL

Kinase Assay ^[2]	<p>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.</p>
Cell Assay ^[2]	<p>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 IC₅₀ values^[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>
Animal Administration ^[1]	<p>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 1×10⁶ 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 mm³. 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.</p>

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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Caution: Product has not been fully validated for medical applications. For research use only.

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