PCI-34051

Cat. No.: HY-15224

CAS No.: 950762-95-5

Molecular Formula: $C_{17}H_{16}N_2O_3$

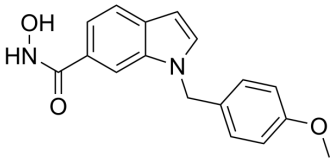
Molecular Weight: 296.32

Target: HDAC; Apoptosis

Pathway: Cell Cycle/DNA Damage; Epigenetics; Apoptosis

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 : ≥ 30 mg/mL (101.24 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	3.3747 mL	16.8736 mL	33.7473 mL
	5 mM	0.6749 mL	3.3747 mL	6.7495 mL
	10 mM	0.3375 mL	1.6874 mL	3.3747 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 (8.44 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (8.44 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (8.44 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

PCI-34051 is a potent and selective HDAC8 inhibitor with IC_{50} of 10 nM, with >200-fold selectivity over the other HDAC isoforms.

IC_{50} & Target	HDAC8	HDAC6	HDAC1	HDAC10
	10 nM (IC_{50})	2.9 μM (IC_{50})	4 μM (IC_{50})	13 μM (IC_{50})

In Vitro	PCI-34051 inhibits pure recombinant HDAC8 with K_i of 10 nM with >200-fold selectivity over the other HDACs tested, including HDACs 1, 2, 3, 6 and 10. PCI-34051 is derived from a low molecular weight hydroxamic acid scaffold that possessed promising potency (HDAC8; K_i=2 μM) and selectivity (approximately fivefold) for HDAC8 relative to the other class I HDACs. PCI-34051 is found to induce apoptosis at low micromolar concentrations in cell lines derived from T-cell lymphomas, including Jurkat and HuT78, whereas doses as high as 20 μM has no effect on B-cell- or myeloid-derived lymphomas or solid tumor lines[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Administration of PCI-34051 and Dexamethasone reduces the eosinophilic inflammation and airway hyperresponsiveness in asthma to reduce the airway remodeling[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	Histone deacetylase activity is measured using a continuous trypsin-coupled assay. For inhibitor characterization, measurements are performed in a reaction volume of 100 μL^{-1} using 96-well assay plates in a fluorescence plate reader. For each isozyme, the HDAC protein in reaction buffer (50 mM HEPES, 100 mM KCl, 0.001% Tween-20, 5% DMSO, pH 7.4, supplemented with bovine serum albumin at concentrations of 0-0.05%) is mixed with inhibitor at various concentrations and allowed to incubate for 15 min. Trypsin is added to a final concentration of 50 nM, and acetyl-Gly-Ala-(N-acetyl-Lys)-amino-4-methylcoumarin is added to a final concentration of 25-100 μM to initiate the reaction. After a 30 min lag time, the fluorescence is measured over a 30 min time frame using an excitation wavelength of 355 nm and a detection wavelength of 460 nm. The increase in fluorescence with time is used as the measure of the reaction rate. Inhibition constants K_i(app) are obtained using the program BatchK_i[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [1]	Tumor cell lines and human umbilical vein endothelial cells are cultured for at least two doubling times, and growth is monitored at the end of compound exposure using an Alamar Blue fluorometric cell proliferation assay as recommended by the manufacturer. Compounds (e.g.,PCI-34051) are assayed in triplicate wells in 96-well plates. The concentration required to inhibit cell growth by 50% (GI_{50}) and 95% confidence intervals are estimated from nonlinear regression using a four-parameter logistic equation[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [2]	Mice[2] A mouse model of asthma is utilized. Briefly, healthy female BALB/C mice (n=72) aged 6-8 weeks and weighing 18-22 g are used. Animals are housed independently in a pathogen-free room and provided ad libitum access to water and standard food. Animals are housed for 1 week prior to experiment onset. Mice are divided into six treatment groups: normal control, simple asthma, Dexamethasone, Tubastatin A HCl, PCI-34051, and Givinostat. Sensitization is carried out for mice in the last five groups on the 1st, 8th and 15th day using ovalbumin (OVA, 20 μg) and aluminum hydroxide gel (2 mg). 7 days after the last sensitization, OVA (20 mg/mL) atomization is performed using an ultrasonic atomizing device (3 mL/min for 30 min, 3 times/week for 8 weeks). Dexamethasone (2.0 mg/kg), TSA (0.5 mg/kg), PCI-34051 (0.5 mg/kg) and Givinostat (0.5 mg/kg) are administered via intraperitoneal injection 30 min before excitation. In the normal control group, normal saline is used instead of OVA. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cell Metab. 2021 Nov 20;S1550-4131(21)00532-5.
- Nucleic Acids Res. 2020 Apr 6;48(6):2912-2923.
- Theranostics. 2021 Mar 20;11(11):5605-5619.

- Clin Transl Med. 15 September 2021.
- Cell Death Dis. 2022 Aug 17;13(8):717.

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REFERENCES

[1]. Balasubramanian S, et al. A novel histone deacetylase 8 (HDAC8)-specific inhibitor PCI-34051 induces apoptosis in T-cell lymphomas. Leukemia. 2008 May;22(5):1026-34.

[2]. Ren Y, et al. Therapeutic effects of histone deacetylase inhibitors in a murine asthma model. Inflamm Res. 2016 Dec;65(12):995-1008.

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