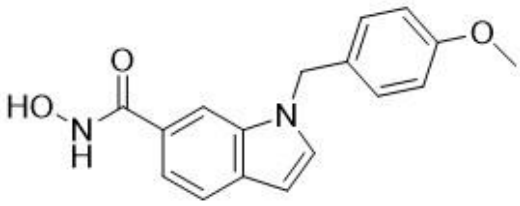
Product data sheet

MedKoo Cat#: 406284 Name: PCI-34051 CAS#: 950762-95-5 Chemical Formula: $C_{17}H_{16}N_2O_3$ Exact Mass: 296.1161 Molecular Weight: 296.32	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:

PCI-34051 is a potent, histone deacetylase 8 (HDAC8)-specific inhibitor with >200-fold selectivity over the other HDAC isoforms. PCI-34051 induces caspase-dependent apoptosis in cell lines derived from T-cell lymphomas or leukemias, but not in other hematopoietic or solid tumor lines. Unlike broad-spectrum HDAC inhibitors, PCI-34051 does not cause detectable histone or tubulin acetylation. PCI-34051 could offer benefits including a greater therapeutic index for treating T-cell malignancies.

2. CoA, QC data, SDS, and handling instruction

SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	30.0	101.2

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	3.37 mL	16.87 mL	33.75 mL
5 mM	0.67 mL	3.37 mL	6.75 mL
10 mM	0.34 mL	1.69 mL	3.37 mL
50 mM	0.07 mL	0.34 mL	0.67 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator

Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study

In vitro study

1.Ha SD, Han CY, Reid C, Kim SO. HDAC8-mediated epigenetic reprogramming plays a key role in resistance to anthrax lethal toxin-induced pyroptosis in macrophages. J Immunol. 2014 Aug 1;193(3):1333-43. doi: 10.4049/jimmunol.1400420. Epub 2014 Jun 27. PMID: 24973453; PMCID: PMC4108443.

2. Sleiman SF, Olson DE, Bourassa MW, Karuppagounder SS, Zhang YL, Gale J, Wagner FF, Basso M, Coppola G, Pinto JT, Holson EB, Ratan RR. Hydroxamic acid-based histone deacetylase (HDAC) inhibitors can mediate neuroprotection independent of HDAC inhibition. J Neurosci. 2014 Oct 22;34(43):14328-37. doi: 10.1523/JNEUROSCI.1010-14.2014. Erratum in: J Neurosci. 2015 Jan 7;35(1):438. PMID: 25339746; PMCID: PMC4205555.

In vivo study

1. Rettig I, Koeneke E, Trippel F, Mueller WC, Burhenne J, Kopp-Schneider A, Fabian J, Schober A, Fernekorn U, von Deimling A, Deubzer HE, Milde T, Witt O, Oehme I. Selective inhibition of HDAC8 decreases neuroblastoma growth in vitro and in vivo and enhances retinoic acid-mediated differentiation. Cell Death Dis. 2015 Feb 19;6(2):e1657. doi: 10.1038/cddis.2015.24. PMID: 25695609; PMCID: PMC4669789.

2. Li ML, Su XM, Ren Y, Zhao X, Kong LF, Kang J. HDAC8 inhibitor attenuates airway responses to antigen stimulus through synchronously suppressing galectin-3 expression and reducing macrophage-2 polarization. Respir Res. 2020 Feb 28;21(1):62. doi: 10.1186/s12931-020-1322-5. PMID: 32111211; PMCID: PMC7048058.

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7. Bioactivity

Biological target:

PCI-34051 is a potent and selective HDAC8 inhibitor with IC50 of 10 nM

In vitro activity

To refine the understanding of which HDACs are relevant in oxidative stress-induced neurodegeneration, an in vitro model of neuronal oxidative death was established. To investigate the role of HDAC8 in oxidative stress-induced neuronal death directly, HDAC8 gene expression was reduced using RNA interference. PCI-34051 was able to significantly protect the cells even when HDAC8 levels were reduced, suggesting that PCI-34051's neuroprotective effect is independent from HDAC8 inhibition. To rule out that the neuroprotective effect of PCI-34051 is dependent on its ability to inhibit residual HDAC8 activity in the knockdown cells, it was reasoned that, if PCI-34051 mediates neuroprotection by inhibiting residual HDAC8 activity in the HDAC8 knockdown cells, then it would be expected to observe that lower doses of PCI-34051 significantly mediate neuroprotection in HDAC8 knockdown cells compared with wild-type cells. Indeed, no changes were observed in the PCI-34051 neuroprotective dose–response, suggesting that the compound's neuroprotective effect is independent from inhibition of residual HDAC8 activity

J Neurosci. 2014 Oct 22; 34(43): 14328–14337. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4205555/

In vivo activity

This study was to investigate the effects of HDAC8 inhibitor PCI-34051 on OVA-exposed lungs and IL-4 treated macrophages Mice were sensitized and then treated with budesonide (BUD) or PCI-34051 (PCI) prior to exposing to normal saline (NS) or ovalbumin (OVA). AHR and airway allergic inflammation were measured in mice exposed to either NS or OVA in presence and absence of BUD or PCI-34051, respectively. The ranking for the resistance measured from concentration-response curves was shown in such an order of OVA > PCI-34051 = BUD > NS in the airflow changes form the investigated animals. In contrast, the average value of Penn from OVA-challenged mice was a three-fold higher than the control mice at the highest dose of MCh (Fig.1a). Although treatment with BUD and PIC resulted in obvious decreases in airway resistance in the animals exposed to OVA, the values were still higher than the control. In statistical analysis, there were significant differences in the values measured at the dosage levels (12.5, 25 and 50 mg/ml) of MCh inhalation between OVA group and other groups (all $P < 0.01$, $n = 6$). Additionally, there were differences seen in the Penh values at the maximum dose of MCh challenge between NS-treated mice and BUD- or PCI-treated ones ($P < 0.05$, $n = 6$). In histopathological examination, representative images of lung sections showed more severe infiltration of peribronchial inflammatory cells and a large amount of mucus secretion in the OVA-exposed lungs than the NS-treated lungs. Treatment with BUD and PCI-34051 resulted in significant reduction in the cell infiltration and mucus accumulation in the challenged lungs (Fig.11d).

Respir Res. 2020; 21: 62. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7048058/