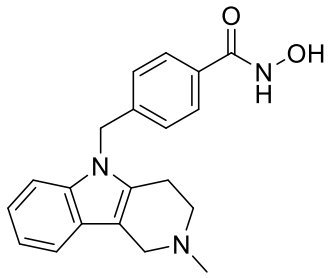
Product data sheet

MedKoo Cat#: 403550 Name: Tubastatin A CAS#: 1252003-15-8 (free base) Chemical Formula: $C_{20}H_{21}N_3O_2$ Exact Mass: 335.16338 Molecular Weight: 335.4	
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:
Tubastatin A is a potent and selective HDAC6 inhibitor. Tubastatin A demonstrates 1093-fold selectivity over HDAC1 (IC50 values of 15 nM for HDAC6 vs 16.4 μM for HDAC1). Tubastatin A was substantially more selective than the known HDAC6 inhibitor Tubacin at all isozymes except HDAC8. Tubastatin A is a potent HDAC6 inhibitor with an IC50 value of 15 nM. Comparatively, it demonstrates over 1,000-fold selectivity against all other HDAC isoforms (IC50 >16 μM), excluding HDAC8 (IC50= 0.9 μM). Tubastatin A induces α-tubulin hyperacetylation at 2.5 μM in primary cortical neuron cultures. In a model of oxidative stress induced by glutathione depletion, tubastatin A displays dose-dependent neuronal protection of primary cortical neuron cultures at 5-10 μM.

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	12.5	37.27

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.98 mL	14.91 mL	29.82 mL
5 mM	0.60 mL	2.98 mL	5.96 mL
10 mM	0.30 mL	1.49 mL	2.98 mL
50 mM	0.06 mL	0.30 mL	0.60 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. Gradilone SA, Radtke BN, Bogert PS, Huang BQ, Gajdos GB, LaRusso NF. HDAC6 inhibition restores ciliary expression and decreases tumor growth. Cancer Res. 2013 Apr 1;73(7):2259-70. doi: 10.1158/0008-5472.CAN-12-2938. Epub 2013 Jan 31. PMID: 23370327; PMCID: PMC3768151.

In vivo study

1. Gradilone SA, Radtke BN, Bogert PS, Huang BQ, Gajdos GB, LaRusso NF. HDAC6 inhibition restores ciliary expression and decreases tumor growth. Cancer Res. 2013 Apr 1;73(7):2259-70. doi: 10.1158/0008-5472.CAN-12-2938. Epub 2013 Jan 31. PMID: 23370327; PMCID: PMC3768151.

2. Fu Z, Kong Q, Wu Y, Hu X, Shi J. Effect of Tubastatin A on the Functional Recovery of Cauda Equina Injury in Rats. World Neurosurg. 2018 Jun;114:e35-e41. doi: 10.1016/j.wneu.2018.01.190. Epub 2018 Feb 3. PMID: 29408594.

7. Bioactivity

Product data sheet

Biological target:

Tubastatin A is a potent and selective HDAC6 inhibitor with an IC50 of 15 nM in a cell-free assay, and is selective (1000-fold more) against all other isozymes except HDAC8 (57-fold more).

In vitro activity

Since HDAC6 overexpression seems to contribute importantly to CCA ciliary lost, HDAC6 expression was inhibited with the HDAC6 inhibitor, tubastatin-A. This approaches induced an increase in acetylated-α-tubulin levels, and the restoration of primary cilia expression in the CCA cell lines (3.3 and 18 –fold, respectivelly) (Figure 5A, D, and E); and the restoration of primary cilia correlated with downregulated Hh and MAPK signaling pathways (Figure 5C), as well as decreased cell proliferation rates (decresed in average by 50%) (Figure 5B and F) and invasion (decreased by 40%) (Figure 5G). To analyze if the restoration of cilia is a major reason for these phenotypic changes, the experiments were repeated in KMCH cells stably transfected with IFT88-shRNA to prevent ciliogenesis. In the experiments in which CCA cells were prevented from developing cilia, the proliferation rates and anchorage-independent growth rates were not significantly different from the vehicle-treated cells (Figure 6A and B), showing that the ability of cells to undergo ciliogenesis is essential for the effects of tubastatin-A.

Reference: Cancer Res. 2013 Apr 1;73(7):2259-70. doi: 10.1158/0008-5472.
https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/23370327/

In vivo activity

The effect of tubastatin-A was tested using a recently developed syngeneic rat orthotopic model of CCA. Tumors were removed after treatment with tubastatin-A or vehicle for 7 days. The mean tumor weights in animals treated with tubastatin-A was 6-fold lower than vehicle-treated controls (0.33 ± 0.09 vs. 1.81 ± 0.51 g, $P<0.05$), and the ratios of tumor weight to liver weight and body weight were also significantly reduced (5-and 5.6-fold, respectively) by tubastatin-A treatment (Figure 7A, B, C, D). Furthermore, confocal immunofluorescence microscopy showed a greater frequency of ciliated cholangiocytes in the treated animals compared with controls (29% vs 1.4% ciliated cells per high power field) (Figure 7E, G). Finally, the amount of PCNA positive cells were significantly reduced in the treated tumors compared with vehicle controls (34% vs 65% PCNA positive cells per high power field), indicating decreased proliferation (Figure 7F, H). These data indicate that a drug that inhibits HDAC6 can significantly reduce the growth of CCA in vivo.

Reference: Cancer Res. 2013 Apr 1;73(7):2259-70. doi: 10.1158/0008-5472.
https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/23370327/