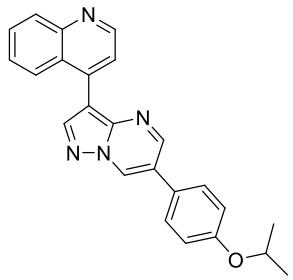
Product data sheet

MedKoo Cat#: 406555 Name: DMH-1 CAS#: 1206711-16-1 Chemical Formula: $C_{24}H_{20}N_4O$ Exact Mass: 380.16371 Molecular Weight: 380.44	
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:
DMH-1 is a second-generation small molecule BMP inhibitor based on dorsomorphin. DMH-1 effectively inhibits the bone morphogenic protein (BMP) ALK2 receptor (IC50 = 108 nM). Treatment with DMH1 reduced lung metastasis and the tumors were less proliferative and more apoptotic. In the surrounding tumor microenvironment, treatment with DMH1 altered fibroblasts, lymphatic vessels and macrophages to be less tumor promoting. These results indicate that inhibition of BMP signaling may successfully target both the tumor and the surrounding microenvironment to reduce tumor burden and metastasis.

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	11.5	30.23

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.63 mL	13.14 mL	26.29 mL
5 mM	0.53 mL	2.63 mL	5.26 mL
10 mM	0.26 mL	1.31 mL	2.63 mL
50 mM	0.05 mL	0.26 mL	0.53 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. Hao J, Lee R, Chang A, Fan J, Labib C, Parsa C, Orlando R, Andresen B, Huang Y. DMH1, a small molecule inhibitor of BMP type i receptors, suppresses growth and invasion of lung cancer. PLoS One. 2014 Mar 6;9(6):e90748. doi: 10.1371/journal.pone.0090748. PMID: 24603907; PMCID: PMC3946239.

2. Sheng Y, Sun B, Xie X, Li N, Dong D. DMH1 (4-[6-(4-isopropoxyphenyl)pyrazolo[1,5-a]pyrimidin-3-yl]quinoline) inhibits chemotherapeutic drug-induced autophagy. Acta Pharm Sin B. 2015 Jul;5(4):330-6. doi: 10.1016/j.apsb.2014.12.010. Epub 2015 Feb 21. PMID: 26579463; PMCID: PMC4629267.

In vivo study

1. Hao J, Lee R, Chang A, Fan J, Labib C, Parsa C, Orlando R, Andresen B, Huang Y. DMH1, a small molecule inhibitor of BMP type i receptors, suppresses growth and invasion of lung cancer. PLoS One. 2014 Mar 6;9(6):e90748. doi: 10.1371/journal.pone.0090748. PMID: 24603907; PMCID: PMC3946239.

7. Bioactivity

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Biological target:

DMH1 is a selective BMP receptor inhibitor with IC50 of 107.9 nM for ALK2, exhibiting no inhibition on AMPK, ALK5, KDR (VEGFR-2) or PDGFR.

In vitro activity

Since cell migration and invasion are known to play an important role in the progression of cancer metastasis, the effects of DMH1 on NSCLC cell migration and invasion were examined in vitro. The scratch-wound assay was used to determine NSCLC cell migration by creating wound gaps in the cultured A549 cells. Cells were then treated with DMSO or DMH1 for 24 hours respectively, and the gap distances were then normalized with the initially measured distances. As shown in Figure 2A and 2B, DMH1 dramatically slowed down migration in a dose-dependent manner. Similar effects of DMH1 on cell migration were also observed in another NSCLC cell line H460 (Figure 2C). In addition, the effect of DMH1 on cell invasion was examined by using modified Boyden chamber assay. A549 cells were seeded on matrigel-coated chambers, followed by 24-h incubation with or without DMH1. 3 μM DMH1 dramatically reduced A549 cell invasion through matrigel-coated membranes by about 52% in comparison with the vehicle controls (Figure 2D).

Referenece: PLoS One. 2014 Mar 6;9(6):e90748. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/24603907/

In vivo activity

The effect of DMH1 on lung tumor cell growth was examined in vivo. The A549 cells were subcutaneously inoculated in the two sides of lower rear flanks of Severe combined immunodeficiency (SCID) mice. Intraperitoneal (i.p.) injections of vehicle (12.5% 2-hydroxypropyl-β-cyclodextrin, n=5) or 5 mg/kg DMH1 (n=5) were initiated on the same day of tumor cell implantation and were performed every other day for 4 weeks. Tumor volumes were measured regularly starting on the sixth day after implantation. The tumor growth was fit into an exponential growth curve (Figure 4A) (R^2 =0.87 and 0.84 for the DMH1 treated and control mice, respectively). The result indicated that the rate for doubling tumor size in DMH1-treated mice was about one day longer than the controls (5.6 versus 4.7 days in the DMH1 treated and control mice, respectively) (Figure 4A). As the initial tumor volumes were similar, no statistical differences between the two groups were observed until day 25. At the end of 4-week treatment, DMH1 treatment resulted in a statistically significant reduction in tumor volumes by about 50% compared to the vehicle control group (p-value <0.05) (Figure 4B). The mouse body weights were measured every other day throughout the experiment, and no notable weight changes were observed in both the control and DMH1 treated groups, suggesting an absence of DMH1 toxic effect at the administered dose (data not shown). To further examine the effect of DMH1 on tumor cell proliferation in vivo, tumor tissue samples from both the vehicle control and DMH1 treatment groups were subjected to Hematoxylin and eosin-stained (H&E) and human specific Ki67 staining. H&E sections were examined for regions that contained tumor and stromal cells, and the result indicated both the vehicle and DMH1 treated groups consisted of a morphologically similar differentiated adenocarcinoma (data not shown). However, immunohistochemical study showed a conspicuously significant decrease of human proliferation marker Ki67 in the DMH1 treated versus vehicle groups, suggesting that DMH1 treatment may attenuate human A549 cancer cell proliferation in vivo (Figure 4C).

Referenece: PLoS One. 2014 Mar 6;9(6):e90748. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/24603907/