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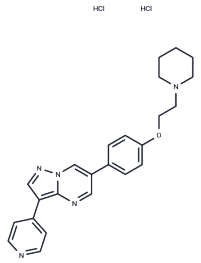
Data Sheet (Cat.No.T6146)

TargetMol

Dorsomorphin dihydrochloride

Chemical Properties



CAS No. : 1219168-18-9

Formula: C24H25N5O¡¤2HCl

Molecular Weight: 472.41

Appearance: no data available

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year

Biological Description

Description	Dorsomorphin dihydrochloride (BML-275 2HCl) is a potent, selective and ATP-competitive AMPK inhibitor (Ki: 109 nM) and does not exhibit significant activity on structurally related kinases.
Targets(IC50)	AMPK,Autophagy,TGF-beta/Smad
In vitro	Dorsomorphin (compound C) is a potent reversible inhibitor that is competitive with ATP, with Ki = 109 ± 16 nM in the absence of AMP. Incubation of cultured hepatocytes with compound C inhibited ACC inactivation by either AICAR or metformin [1]. Compound C suppressed 2-deoxy-D-glucose (2DG)-induced GRP78 promoter activity in a dose-dependent manner but had little effect on tunicamycin-induced GRP78 promoter activity. Compound C also suppressed GRP78 promoter activity induced by glucose withdrawal [2].
In vivo	6 h after dorsomorphin was administered intravenously, hepatic hepcidin mRNA levels were reduced to one-third of that of vehicle-injected mice. Alterations in hepcidin levels affect serum iron concentrations within 24 h via the altered mobilization of intracellular iron by ferroportin33. Administration of dorsomorphin over 24 h led to a 60% increase in total serum iron concentrations [3].
Kinase Assay	Liver AMPK was partially purified from male SD rats to the blue-Sepharose step. The 100-µl reaction mixture contained 100 µM AMP, 100 µM ATP (0.5 µCi 33P-ATP per reaction), and 50 µM SAMS in a buffer (40 mM HEPES, pH 7.0, 80 mM NaCl, 0.8 mM EDTA, 5 mM MgCl2, 0.025% BSA, and 0.8 mM DTT). The reaction was initiated with the addition of the enzyme. After a 30-minute incubation at 30°C, the reaction was stopped by addition of 80 µl 1% H3PO4. Aliquots (100 µl) were transferred to 96-well MultiScreen plates. The plate was washed three times with 1% H3PO4 followed by detection in a Top-count. The in vitro AMPK inhibition data obtained with compound C – (6-[4-(2-Piperidin-1-yl-ethoxy)-phenyl)]-3-pyridin-4-yl-pyyrazolo[1,5-a] pyrimidine – were fit to the following equation for competitive inhibition by nonlinear regression using a least-squares Marquardt algorithm in a computer program written by N. Thornberry of Merck Research Laboratories: Vi/Vo = (Km + S)/[S + Km × (1 + I/Ki)], where Vi is the inhibited velocity, Vo is the initial velocity, S is the substrate (ATP) concentration, Km is the Michaelis constant for ATP, I is the inhibitor (compound C) concentration, and Ki is the dissociation constant for compound C [1].
Cell Research	C2C12 cells were seeded into 96-well plates at 2,000 cells per well in DMEM supplemented with 2% FBS. Wells were treated in quadruplicate with BMP ligands and

	dorsomorphin or vehicle. Cells were harvested after 5 d in culture with 50 µl Tris-buffered saline, 1% Triton X-100. Lysates were added to p-nitro-phenylphosphate reagent in 96-well plates for 1 h, and alkaline phosphatase activity expressed as absorbance at 405 nM. Cell viability and quantity were measured by Cell-titer Glo and binding of nuclear dye CyQuant, respectively, using replicate wells treated identically to those used for alkaline phosphatase measurements [3].
Animal Research	12-week-old C57BL/6 mice raised on a standard diet were injected via the tail vein with 0.2 g kg?1 of dextran (average MW = 5,000) or 0.2 g kg?1 of iron-dextran USP. Dextran was injected with vehicle only, whereas iron-dextran was injected with either vehicle or dorsomorphin (10 mg/kg). 1 h after injection, mice were killed and liver segments were collected in 500 µl of SDS-lysis buffer and mechanically homogenized. 20 µl of liver extracts were resolved by SDS-PAGE and immunoblotted. Total RNA was harvested using Trizol from mechanically homogenized mouse livers (6 h after injection with a single intraperitoneal dose of dorsomorphin (10 mg/kg) or DMSO) [3].

Solubility Information

Solubility	DMSO: 6.88 mg/mL (14.55 mM),Sonication is recommended. H2O: 47.2 mg/mL (100 mM), (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.1168 mL	10.584 mL	21.1681 mL
5 mM	0.4234 mL	2.1168 mL	4.2336 mL
10 mM	0.2117 mL	1.0584 mL	2.1168 mL
50 mM	0.0423 mL	0.2117 mL	0.4234 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Reference

Li N, et al. Dorsomorphin induces cancer cell apoptosis and sensitizes cancer cells to HSP90 and proteasome inhibitors by reducing nuclear heat shock factor 1 levels. Cancer Biol Med. 2019 May;16(2):220-233.
Xu J, Ao Y