Dorsomorphin

Cat. No.: HY-13418A

CAS No.: 866405-64-3

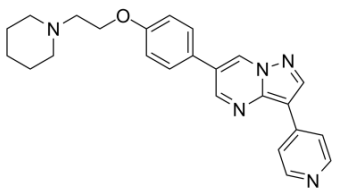
Molecular Formula: $C_{24}H_{25}N_5O$

Molecular Weight: 399.49

Target: AMPK; TGF-β Receptor; Autophagy

Pathway: Epigenetics; PI3K/Akt/mTOR; TGF-beta/Smad; Autophagy

Storage: 4°C, protect from light
* In solvent : -80°C, 6 months; -20°C, 1 month (protect from light)



SOLVENT & SOLUBILITY

In Vitro

1M HCl : 50 mg/mL (125.16 mM; ultrasonic and adjust pH to 1 with HCl)
DMSO : 5 mg/mL (12.52 mM; ultrasonic and warming and heat to 80°C)
Ethanol : 3.33 mg/mL (8.34 mM; Need ultrasonic)
H_2O : 3.33 mg/mL (8.34 mM; ultrasonic and adjust pH to 6 with HCl)
H_2O : 1 mg/mL (2.50 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.5032 mL	12.5160 mL	25.0319 mL
5 mM	0.5006 mL	2.5032 mL	5.0064 mL
10 mM	0.2503 mL	1.2516 mL	2.5032 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 0.5% CMC-Na/saline water
   Solubility: 26 mg/mL (65.08 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 0.2 mg/mL (0.50 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 0.2 mg/mL (0.50 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 0.2 mg/mL (0.50 mM); Clear solution
5. Add each solvent one by one: 10% EtOH >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 0.33 mg/mL (0.83 mM); Clear solution
6. Add each solvent one by one: 10% EtOH >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 0.33 mg/mL (0.83 mM); Clear solution
7. Add each solvent one by one: 10% EtOH >> 90% corn oil
   Solubility: ≥ 0.33 mg/mL (0.83 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Dorsomorphin (Compound C) is a selective and ATP-competitive AMPK inhibitor (K_i=109 nM in the absence of AMP). Dorsomorphin (BML-275) selectively inhibits BMP type I receptors ALK2, ALK3, and ALK6. Dorsomorphin induces autophagy [1][2].

IC_{50} & Target

AMPK	ALK2	ALK3	ALK6
109 nM (Ki)			

Autophagy

In Vitro

Dorsomorphin (compound C) (0-10 μM, 18 h) suppresses 2DG-induced GRP78 promoter activity in human fibrosarcoma HT1080 cells in a dose-dependent manner but has little effect on tunicamycin-induced GRP78 promoter activity. Dorsomorphin (compound C) C also suppresses GRP78 promoter activity induced by glucose withdrawal. Dorsomorphin (compound C) has no effect on 2DG-induced PERK activation and reduces the both basal and 2DG-induced AMPK phosphorylation levels in HT1080 cells[2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Western Blot Analysis[2]

Cell Line:	Human fibrosarcoma HT1080 cells
Concentration:	0-10 μM.
Incubation Time:	18 hours.
Result:	Suppressed 2DG-induced GRP78 promoter activity in a dose-dependent manner and also suppressed GRP78 promoter activity induced by glucose withdrawal.

In Vivo

Dorsomorphin (compound C: 10 mg/kg, intravenously once) treatment leads to a 60% increase in total serum iron concentrations, reduces basal levels of hepcidin expression and increasing serum iron concentrations in adult mice[3].
Dorsomorphin (compound C: 0.2 mg/kg, I.V., 30 min before LPS injection) reduces ICAM-1 and VCAM-1 expression in LPS-injected rat aorta[4].
Dorsomorphin (compound C; 25 mg/kg; i.p. injection; in male BALB/c mice) treatment before lipopolysaccharide (LPS) injection significantly reduces lethality in contrast to animals treated with LPS challenge only[5].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Wild-type (WT) C57BL/6 adult mice that are fed a standard iron-replete diet express high levels of hepcidin[3].
Dosage:	10 mg/kg.
Administration:	Intravenously once.
Result:	Led to a 60% increase in total serum iron concentrations. Effective in reducing basal levels of hepcidin expression and increasing serum iron concentrations in adult mice.

Animal Model:	Male Sprague-Dawley rats, 8 weeks of age (body weight 230-250 g)[4].
Dosage:	0.2 mg/kg.
Administration:	I.V., 30 min before LPS injection.

Result:	Reduced ICAM-1 and VCAM-1 expression in LPS-injected rat aorta.

Animal Model:	Male BALB/c mice at 6-7 weeks of age weighing 20-22 g[5]
Dosage:	25 mg/kg
Administration:	Injection i.p.; 60 min before LPS challenge
Result:	Treatment of mice with 25 mg/kg before LPS injection significantly reduced lethality in contrast to animals treated with LPS challenge only.

CUSTOMER VALIDATION

- Nat Nanotechnol. 2021 May 6.
- Cell Metab. 2021 Mar 2;33(3):565-580.e7.
- Mol Cell. 2020 Jan 2;77(1):95-107.e5.
- Mol Cell. 2017 Oct 19;68(2):336-349.e6.
- Redox Biol. 2018 Oct;19:339-353.

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REFERENCES

[1]. Zhou G, et al. Role of AMP-activated protein kinase in mechanism of action. J Clin Invest. 2001 Oct;108(8):1167-74.

[2]. Saito S, et al. Compound C prevents the unfolded protein response during glucose deprivation through a mechanism independent of AMPK and BMP signaling. PLoS One. 2012;7(9):e45845.

[3]. Yu PB, et al. Dorsomorphin inhibits BMP signals required for embryogenesis and iron metabolism. Nat Chem Biol. 2008 Jan;4(1):33-41.

[4]. Kim YM, et al. Compound C independent of AMPK inhibits ICAM-1 and VCAM-1 expression in inflammatory stimulants-activated endothelial cells in vitro and in vivo. Atherosclerosis. 2011 Nov;219(1):57-64.

[5]. Guo Y, et al. AMPK inhibition blocks ROS-NFκB signaling and attenuates endotoxemia-induced liver injury. PLoS One. 2014 Jan 24;9(1):e86881.

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