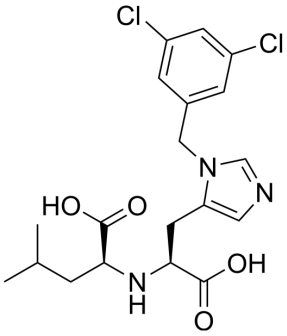
MLN-4760

Cat. No.:	HY-19414
CAS No.:	305335-31-3
Molecular Formula:	$C_{19}H_{23}Cl_2N_3O_4$
Molecular Weight:	428.31
Target:	Angiotensin-converting Enzyme (ACE)
Pathway:	Metabolic Enzyme/Protease
Storage:	4°C, stored under nitrogen, away from moisture * In solvent : -80°C, 6 months; -20°C, 1 month (stored under nitrogen, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

H_2O : 100 mg/mL (233.48 mM; Need ultrasonic)
DMSO : 50 mg/mL (116.74 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.3348 mL	11.6738 mL	23.3476 mL
5 mM	0.4670 mL	2.3348 mL	4.6695 mL
10 mM	0.2335 mL	1.1674 mL	2.3348 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (5.84 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.84 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.84 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

MLN-4760 is a potent and selective human ACE2 inhibitor (IC_{50}, 0.44 nM), with excellent selectivity (>5000-fold) versus related enzymes including human testicular ACE (IC_{50}, >100 μM) and bovine carboxypeptidase A (CPDA; IC_{50}, 27 μM).

IC_{50} & Target

IC50: 0.44 nM (Human ACE2), 27 μM (Bovine carboxypeptidase A)[1]

In Vitro

MLN-4760 is a potent and selective human ACE2 inhibitor (IC_{50}, 0.44 nM), with excellent selectivity (>5000-fold) versus related enzymes human testicular ACE (IC_{50}, >100 μM) and bovine carboxypeptidase A (CPDA; IC_{50}, 27 μM)[1].

	MLN-4760 effectively quenches cleavage of the 7-Mca-YVADAPK(Dnp) in rhACE2. MLN-4760 shows pIC_{50} at rhACE2 of 8.5±0.1 and at rhACE of 4.4±0.2. MLN-4760 also shows pIC_{50} at rhACE2 of 4.7±0.1, 6.9±0.1 and at ACE of 4.4±0.1, 6.2±0.1 in murine heart and mononuclear cells (MNCs), reseptively[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	MLN-4760 (100 μM, intracerebroventricular infusion for five days) significantly worsens neurological function at 4 h and 3 d post-stroke without significantly increasing infarct volume[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [3]	Rats[3] In a related experiment to evaluate the role of central ACE2 in stroke, randomly assigned rats (n = 16) are treated centrally for five days prior to and three days after stroke with the ACE2 inhibitor MLN-4760 (100 μM infused at a rate of 0.5 μL/h) or sterile saline (0.9%) via intracerebroventricular infusion. Following endothelin-1 MCAO, neurological function is assessed at 4 h, 1 d, and 3 d, and brains are harvested at 3 d post-stroke for infarct volume analysis as above[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Acta Pharm Sin B. 2021 Jan;11(1):222-236.
- Biol Res. 2023 Oct 25;56(1):55.
- Int J Pharm. 2023 Sep 30:123453.
- Infect Dis Ther. 2021 Feb 2;1-12.
- Cell Signal. 2022 Jul 23;110418.

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REFERENCES

[1]. Dales NA, et al. Substrate-based design of the first class of angiotensin-converting enzyme-related carboxypeptidase (ACE2) inhibitors. J Am Chem Soc. 2002 Oct 9;124(40):11852-3.

[2]. Joshi S, et al. Angiotensin converting enzyme versus angiotensin converting enzyme-2 selectivity of MLN-4760 and DX600 in human and murine bone marrow-derived cells. Eur J Pharmacol. 2016 Mar 5;774:25-33.

[3]. Bennion DM, et al. Activation of the Neuroprotective Angiotensin-Converting Enzyme 2 in Rat Ischemic Stroke. Hypertension. 2015 Jul;66(1):141-8.

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