Fasudil Hydrochloride

Cat. No.: HY-10341

CAS No.: 105628-07-7

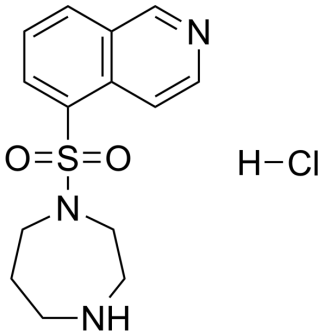
Molecular Formula: $C_{14}H_{18}ClN_3O_2S$

Molecular Weight: 327.83

Target: ROCK; Calcium Channel; Autophagy; PKA; PKC; HIV

Pathway: Cell Cycle/DNA Damage; Cytoskeleton; Stem Cell/Wnt; TGF-beta/Smad; Membrane Transporter/Ion Channel; Neuronal Signaling; Autophagy; Epigenetics; Anti-infection

Storage: 4°C, sealed storage, away from moisture
* In solvent : -80°C, 1 year; -20°C, 6 months (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

H_2O : 55 mg/mL (167.77 mM; Need ultrasonic)
DMSO : ≥ 31 mg/mL (94.56 mM)
* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	3.0504 mL	15.2518 mL	30.5036 mL
5 mM	0.6101 mL	3.0504 mL	6.1007 mL
10 mM	0.3050 mL	1.5252 mL	3.0504 mL

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

In Vivo

1. Add each solvent one by one: PBS
   Solubility: 100 mg/mL (305.04 mM); Clear solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (6.34 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (6.34 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (6.34 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Fasudil (HA-1077; AT877) Hydrochloride is a nonspecific RhoA/ROCK inhibitor and also has inhibitory effect on protein kinases, with an K_i of 0.33 μM for ROCK1, IC_{50}s of 0.158 μM and 4.58 μM, 12.30 μM, 1.650 μM for ROCK2 and PKA, PKC, PKG, respectively. Fasudil Hydrochloride is also a potent Ca^{2+} channel antagonist and vasodilator[1][2][3].

IC_{50} & Target	p160ROCK 0.33 μM (Ki)	ROCK2 0.158 μM (IC_{50})	PKA 4.58 μM (IC_{50})	PKC 12.30 μM (IC_{50})
	PKG 1.65 μM (IC_{50})			

In Vitro

Fasudil Hydrochloride (100 μM) inhibits cell spreading, the formation of stress fibers, and expression of α-SMA with concomitant suppression of cell growth in rat HSCs (hepatic stellate cells) and human HSC-derived TWNT-4 cells[4].
Fasudil Hydrochloride (50-100 μM; 24 hours) inhibits the LPA (lysophoaphatidic acid)-induced phosphorylation of ERK1/2, JNK, and p38 detected by western blotting in rat HSCs and human HSC-derived TWNT-4 cells[4].
Fasudil Hydrochloride (25-100 μM; 24 hours) suppresses transcription of collagen and TIMP, stimulates transcription of MMP-1 in human HSC-derived TWNT-4 cells[4].

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

Western Blot Analysis[4]

Cell Line:	Rat HSCs and human HSC-derived TWNT-4 cells
Concentration:	50 μM; 100 μM
Incubation Time:	24 hours
Result:	Suppressed the LPA-induced phosphorylation of ERK1/2, JNK and p38 MAPK by 60%, 70%,and 90%, respectively.

RT-PCR[4]

Cell Line:	Rat HSCs and human HSC-derived TWNT-4 cells
Concentration:	25 μM; 50 μM; 100 μM 24 hours
Incubation Time:	24 hours
Result:	Reduced the expression of type I collagen, a-SMA, and TIMP-1.

In Vivo

Fasudil Hydrochloride (10 mg/kg; i.v.; 1 h before operation) exhibits protectable effects on cardiovascular disease and reduces the activation of JNK and attenuates mitochondrial-nuclear translocation of AIF under ischemic injury[5].
Fasudil Hydrochloride (50 mg/kg/d; i.p.) inhibits acute and relapsing EAE (experimental autoimmune encephalomyelitis) induced by proteolipid protein PLP p139-151, reduces lymphocytes proliferation, results downregulation of interleukin (IL)-17 and a marked decrease of the IFN-γ/IL-4 ratio[6].
Fasudil Hydrochloride (100 mg/kg/d; p.o.) significantly reduces incidence and pathological examination score of EAE (experimental autoimmune encephalomyelitis) in SJL/J mice, decreases inflammation, demyelination, axonal loss and APP positivein spinal cord in mice[6].

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

Animal Model:	Myocardial ischemia and reperfusion in rat (250-300 g)[5]
Dosage:	10 mg/kg
Administration:	Intravenous injection; 1 h before operation
Result:	Activated the Rho-kinase, JNK, and resulted AIF translocated to the nucleus. Inhibited Rho-kinase activity, and reduced myocardial infarct size and heart cell apoptosis.

CUSTOMER VALIDATION

- Cell Mol Immunol. 2023 Mar 2;1-14.
- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- J Exp Clin Cancer Res. 2020 Jun 16;39(1):113.
- Clin Transl Med. 2022 Oct;12(10):e1036.
- Clin Transl Med. 2022 Jul;12(7):e961.

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REFERENCES

[1]. Chen M, et al. Fasudil and its analogs: a new powerful weapon in the long war against central nervous system disorders? Expert Opin Investig Drugs. 2013 Apr;22(4):537-50.

[2]. Huang XN, et al. The effects of fasudil on the permeability of the rat blood-brain barrier and blood-spinal cordbarrier following experimental autoimmune encephalomyelitis. J Neuroimmunol. 2011 Oct 28;239(1-2):61-7.

[3]. Uehata M, et al. Calcium sensitization of smooth muscle mediated by a Rho-associated protein kinase in hypertension. Nature. 1997 Oct 30;389(6654):990-4.

[4]. Fukushima M, et al. Fasudil hydrochloride hydrate, a Rho-kinase (ROCK) inhibitor, suppresses collagen production and enhances collagenase activity in hepatic stellate cells. Liver Int. 2005 Aug;25(4):829-38.

[5]. Corbin KD, et al. Choline metabolism provides novel insights into nonalcoholic fatty liver disease and its progression. Curr Opin Gastroenterol. 2012 Mar;28(2):159-65.

[6]. Zhang J, et al. Inhibition of the activity of Rho-kinase reduces cardiomyocyte apoptosis in heart ischemia/reperfusion via suppressing JNK-mediated AIF translocation. Clin Chim Acta. 2009 Mar;401(1-2):76-80.

[7]. Sun X, et al. The selective Rho-kinase inhibitor Fasudil is protective and therapeutic in experimental autoimmune encephalomyelitis. J Neuroimmunol. 2006 Nov;180(1-2):126-34. Epub 2006 Sep 22.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA