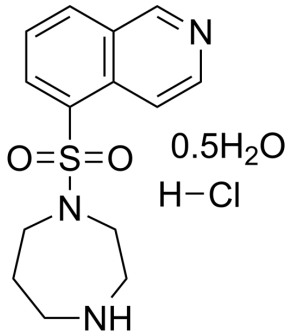
Fasudil hydrochloride semihydrate

Cat. No.:	HY-10341B
CAS No.:	186694-02-0
Molecular Formula:	$C_{14}H_{19}ClN_3O_{2.5}S$
Molecular Weight:	673.68
Target:	ROCK; Calcium Channel; Autophagy; HIV; PKA; PKC
Pathway:	Cell Cycle/DNA Damage; Cytoskeleton; Stem Cell/Wnt; TGF-beta/Smad; Membrane Transporter/Ion Channel; Neuronal Signaling; Autophagy; Anti-infection; Epigenetics
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

Fasudil (HA-1077; AT877) hydrochloride semihydrate 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 semihydrate is also a potent Ca^{2+} channel antagonist and vasodilator[1][2][3].

IC_{50} & Target

PKA 4.58 μM (IC_{50})	p160ROCK 0.33 μM (Ki)	ROCK2 0.158 μM (IC_{50})	PKC 12.3 μM (IC_{50})
PKG 1.65 μM (IC_{50})			

In Vitro

Fasudil hydrochloride semihydrate (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 semihydrate (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 semihydrate (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

Incubation Time:	24 hours
Result:	Reduced the expression of type I collagen, a-SMA, and TIMP-1.

In Vivo

Fasudil hydrochloride semihydrate (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 semihydrate (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 semihydrate (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

- 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.
- Br J Cancer. 2023 Mar 23.

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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]. 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.

[6]. 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.

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