SAR407899 hydrochloride

Cat. No.: HY-15687

CAS No.: 923262-96-8

Molecular Formula: $C_{14}H_{17}ClN_2O_2$

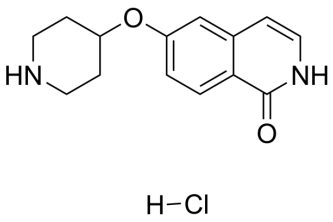
Molecular Weight: 280.75

Target: ROCK

Pathway: Cell Cycle/DNA Damage; Cytoskeleton; Stem Cell/Wnt; TGF-beta/Smad

Storage: 4°C, sealed storage, away from moisture

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



SOLVENT & SOLUBILITY

In Vitro

H_2O : 50 mg/mL (178.09 mM; Need ultrasonic)

DMSO : 25 mg/mL (89.05 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	3.5619 mL	17.8094 mL	35.6189 mL
5 mM	0.7124 mL	3.5619 mL	7.1238 mL
10 mM	0.3562 mL	1.7809 mL	3.5619 mL

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

In Vivo

1. Add each solvent one by one: PBS
   Solubility: 25 mg/mL (89.05 mM); Clear solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (8.90 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (8.90 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (8.90 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

SAR407899 hydrochloride is a selective, potent and ATP-competitive ROCK inhibitor, with an IC_{50} of 135 nM for ROCK-2, and K_is of 36 nM and 41 nM for human and rat ROCK-2, respectively.

IC_{50} & Target	ROCK-2	ROCK-1
	102 nM (IC_{50})	276 nM (IC_{50})

In Vitro	SAR407899 hydrochloride is a potent and ATP-competitive ROCK inhibitor, with K_is of 36 nM and 41 nM for human and rat ROCK-2, respectively. SAR407899 inhibits ROCK-2 better than ROCK-1, with IC_{50}s of 102±19 nM and 276±26 nM, respectively, in the presence of 40 μM ATP. SAR407899 also less potently inhibits PKC-Δ and MSK-1, with IC_{50}s of 5.4 and 3.1 μM, respectively. SAR407899 (0.1, 0.3, 1.0, and 3.0 μM) specifically inhibits the ROCK-mediated phosphorylation of $MYPT^{T696}$ in HeLa cells stimulated with PHEN, and shows such effects at 1 μM and 10 μM in primary rat aortic smooth muscle cells. SAR407899 (3 μM) completely blocks thrombin-induced shrinkage of human umbilical vein endothelial cells (HUVECs) and stress fiber formation. SAR407899 concentration-dependently inhibits 5-bromodeoxyuridine incorporation into the cells with an IC_{50} of 5.0±1.3 μM. SAR407899 also effectively inhibits THP-1 migration with an IC_{50} of 2.5±1.0 μM. SAR407899 shows a potent vasorelaxant activity in a broad variety of isolated arteries taken from different vascular beds and species, with a range of IC_{50} values between 122 and 280 nM[1]. SAR407899 dose-dependently relaxes the phenylephrine pre-contracted smooth muscle, with IC_{50}s of 0.07 and 0.05 μM, respectively[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	SAR407899 (3 mg/kg, i.v.) inhibits ROCK-mediated phosphorylation of $MYPT^{T696}$ in thoracic aorta of spontaneously hypertensive rats (SHRs). SAR407899 (0.01-0.30 mg/kg, i.v.) efficiently reduces pressor responses to vasoconstrictor agents in rats. SAR407899 (1, 3, 10, and 30 mg/kg, p.o.) dose dependently lowers blood pressure in hypertensive SHRs[1]. SAR407899 (1-3 mg/kg, i.v. or 3, 10 mg/kg, p.o.) increases the length of the penis in healthy rabbits. SAR407899 (3-10 mg/kg, p.o.) also dose-dependently increases penile length in diabetic rabbits[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [2]	Rabbits are treated either intravenously (i.v., in an ear vein) with increasing doses of SAR407899 (0.3, 1, 3, 10 mg/kg) or orally with SAR407899 (1, 3, 10, 30 mg/kg) or sildenafil (2 or 6 mg/kg). Each animal is used several times for different doses and different agents, always with a week's washout. The length (mm) of uncovered penile mucosa (penile erection parameter) is measured at different time-points, using a sliding digital caliper. The results are expressed as mean ± SEM penile length of 3-5 rabbits[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Science. 2017 Dec 1;358(6367):eaan4368.
- JCI Insight. 2018 Jun 7;3(11). pii: 98921.

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REFERENCES

[1]. L?hn M, et al. Pharmacological characterization of SAR407899, a novel rho-kinase inhibitor. Hypertension. 2009 Sep;54(3):676-83.

[2]. Guagnini F, et al. Erectile properties of the Rho-kinase inhibitor SAR407899 in diabetic animals and human isolated corpora cavernosa. J Transl Med. 2012 Mar 23;10:59.

[3]. Chen W, et al. Screening RhoA/ROCK inhibitors for the ability to prevent chronic rejection of mouse cardiac allografts.Transpl Immunol. 2018 Jun 6. pii: S0966-3274(18)30029-7.

Caution: Product has not been fully validated for medical applications. For research use only.

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