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产品名称：SAR407899 (hydrochloride)
产品别名：SAR407899 hydrochloride

生物活性：

Description	SAR407899 hydrochloride is a selective, potent and ATP-competitive ROCK inhibitor, with an IC50 of 135 nM for ROCK-2, and Kis 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].	
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].	

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

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

In Vivo:

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 In Vitro 方式配制澄清的储

Solvent&Solubility	备液，再依次添加助溶剂： ——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶 1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline Solubility: ≥ 2.5 mg/mL (8.90 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (8.90 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。 2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline) Solubility: ≥ 2.5 mg/mL (8.90 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (8.90 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.5 mg/mL (8.90 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (8.90 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
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.

实验参考：

Animal Administration	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].
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.