上海源叶生物科技有限公司
Shanghai yuanye Bio-Technology Co., Ltd
电话：021-61312973　　传真：021-55068248
网址：www.shyuanye.com
邮箱：shyysw@sina.com

产品名称：SAR407899
产品别名：SAR407899

生物活性：

Description	SAR407899 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 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].

Solvent&Solubility

In Vitro:

DMSO : 6 mg/mL (24.56 mM; Need warming)

Preparing Stock Solutions	Solvent / Mass / Concentration	**1 mg**	**5 mg**	**10 mg**
	1 mM	4.0935 mL	20.4675 mL	40.9350 mL
	5 mM	0.8187 mL	4.0935 mL	8.1870 mL
	10 mM	0.4093 mL	2.0467 mL	4.0935 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。

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

References	[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.

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]. Löhn 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.