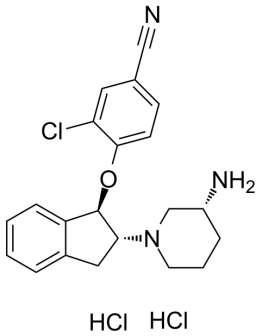
SAR7334 hydrochloride

Cat. No.:	HY-15699A
CAS No.:	1333207-63-8
Molecular Formula:	$C_{21}H_{24}Cl_3N_3O$
Molecular Weight:	440.79
Target:	TRP Channel
Pathway:	Membrane Transporter/Ion Channel; Neuronal Signaling
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

DMSO : 100 mg/mL (226.87 mM; Need ultrasonic)
H_2O : 50 mg/mL (113.43 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.2687 mL	11.3433 mL	22.6865 mL
	5 mM	0.4537 mL	2.2687 mL	4.5373 mL
	10 mM	0.2269 mL	1.1343 mL	2.2687 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (5.67 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.67 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.67 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

SAR7334 hydrochloride is a potent and specific TRPC6 inhibitor, inhibiting TRPC6 currents with IC_{50} of 7.9 nM.

IC_{50} & Target

IC50: 7.9 nM (TRPC6 currents)[3]

In Vitro

SAR7334 inhibits TRPC6, TRPC3 and TRPC7-mediated Ca^{2+} influx into cells with IC_{50}s of 9.5, 282 and 226 nM[1][2][3], whereas TRPC4 and TRPC5-mediated Ca^{2+} entry is not affected. SAR7334 (1 μM) results in a major block of the Ang II-evoked calcium influx in the podocytes[1]. SAR7334 (1 μM) has negligible effect on SOCE[2]. SAR7334 dose-dependently reduces TRPC6 currents with an IC_{50} of 7.9 nM. SAR7334 (100 nM) substantially reduces TRPC6 currents[3].

	MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	SAR7334 (10 mg/kg, p.o.) suppresses TRPC6-dependent acute HPV in isolated perfused lungs from mice. SAR7334 demonstrates that it is suitable for chronic oral administration. In an initial short-term study, SAR7334 does not change mean arterial pressure in spontaneously hypertensive rats (SHR)[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [3]	Adult male (6 months old) spontaneously hypertensive rats (SHR) are treated on two consecutive days. On day one, the animals receive 1 mL/kg vehicle by oral gavage. After 24 h, rats receive either vehicle alone or are treated with 10 mg/kg SAR7334. Telemetric measurement of BP is performed. In brief, a telemetric device (TL11M2-C50-PXT PMP) is placed between the aorta and the vena cava and the catheter tip of the transmitter is inserted into the aorta. Systolic BP, diastolic BP and heart rate are acquired continuously at a sampling rate of 500 Hz and data are stored as 5 min averages. Mean arterial pressure is calculated from systolic and diastolic pressure and low-pass filtered using the fast Fourier transform function of the vendor software for better visualization of time-dependent BP variations. For statistical analysis, raw data are averaged over a 6 h period starting 2 h after application of vehicle or SAR7334. This interval corresponds to the maximal plasma levels of SAR7334. Baseline data are sampled over the same time interval on the day before treatment. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Mol Ther. 2022 Jan 22;S1525-0016(22)00033-8.
- Cell Death Dis. 2020 Mar 5;11(3):170.
- Cell Death Dis. 2018 Oct 3;9(10):1015.
- Cells. 2020 Jan 14;9(1):202.
- J Physiol. 2024 Feb 10.

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REFERENCES

[1]. Ilatovskaya DV, et al. The Role of Angiotensin II in Glomerular Volume Dynamics and Podocyte Calcium Handling. Sci Rep. 2017 Mar 22;7(1):299.

[2]. Chauvet S, et al. Pharmacological Characterization of the Native Store-Operated Calcium Channels of Cortical Neurons from Embryonic Mouse Brain. Front Pharmacol. 2016 Dec 12;7:486.

[3]. Maier T, et al. Discovery and pharmacological characterization of a novel potent inhibitor of diacylglycerol-sensitive TRPC cation channels. Br J Pharmacol. 2015 Jul;172(14):3650-60.

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

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