Product Data Sheet

Product Name: TRPC6 inhibitor
Cat. No.: GC13218

Chemical Properties

Cas. No.	1333207-63-8		
Chemical Name	4-(((1R,2R)-2-((R)-3-aminopiperidin-1-yl)-2,3-dihydro-1H-inden-1-yl)oxy)-3-chlorobenzonitrile dihydrochloride		
SMILES	ClC1=C(O[C@]2([H])C3=CC=CC=C3C[C@@]2([H])N4CCC[C@](N)([H])C4)C=CC(C#N)=C1.Cl.Cl		
Formula	$C_{21}H_{24}Cl_3N_3O$	M.Wt	440.79
Solubility	DMF: 1 mg/mL,DMSO: 15 mg/mL,Ethanol: 25 mg/mL,Ethanol:PBS (pH 7.2) (1:5): 0.16mg/mL	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure	TRPC6 inhibitor		

Protocol

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com
Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

Animal experiment:

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.

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,

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com
Address: 10292 Central Ave. #205, Montclair, CA, USA

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.

Background

SAR7334 hydrochloride is a potent and specific TRPC6 inhibitor, inhibiting TRPC6 currents with IC50 of 7.9 nM.
SAR7334 inhibits TRPC6, TRPC3 and TRPC7-mediated Ca2+ influx into cells with IC50s of 9.5, 282 and 226 nM[1][2][3], whereas TRPC4 and TRPC5-mediated Ca2+ 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 IC50 of 7.9 nM. SAR7334 (100 nM) substantially reduces TRPC6 currents[3].
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].

[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.

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com
Address: 10292 Central Ave. #205, Montclair, CA, USA