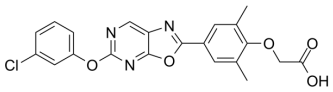
SAR247799

Cat. No.:	HY-115831
CAS No.:	1315311-14-8
Molecular Formula:	$C_{21}H_{16}ClN_3O_5$
Molecular Weight:	425.82
Target:	LPL Receptor
Pathway:	GPCR/G Protein
Storage:	4°C, sealed storage, away from moisture and light * In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture and light)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 33.33 mg/mL (78.27 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.3484 mL	11.7421 mL	23.4841 mL
	5 mM	0.4697 mL	2.3484 mL	4.6968 mL
	10 mM	0.2348 mL	1.1742 mL	2.3484 mL

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

BIOLOGICAL ACTIVITY

Description

SAR247799 (S1P1 agonist 3) is an oral activity, selective G-protein-biased sphingosine-1 phosphate receptor-1 (S1P1) agonist, with EC_{50}s rang from 12.6 to 493 nM in S1P1-overexpressing cells and HUVECs. SAR247799 can be used for the research of endothelial protection, including type-2 diabetes, metabolic syndrome[1][2][3][4].

IC_{50} & Target

S1PR1
12.6-493 nM (EC50)

In Vitro

SAR247799 (0, 0.003, 0.01, 0.03, 0.1, 0.3, 1, 3, 10 μM; 10 min) induces a concentration-dependent phosphorylation of extracellular-regulated kinase-1/2 (Erk1/2) and protein kinase B (Akt) in HUVECs[1].
SAR247799 (0-10 μM, 8 min) induces impedance change in HUVECs in a dose-dependent manner[1].
SAR247799 (1 μM, 1st) does not cause desensitization demonstrated by Ca^{2+} flux assay in S1P1-Chinese hamster ovary (CHO) cells[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

SAR247799 (1 and 3 mg/kg; p.o.; 1 h before renal occlusion) dose dependently reduces the severity of ischemia/reperfusion (I/R)–induced acute kidney injury[1].

SAR247799 (0.3, 1, 3 mg/kg; i.v.) dose dependently increases the coronary conductance ratio in pig model of coronary endothelial dysfunction[1].

SAR247799 (30-min intravenous administration; 8- to 10-week-old farm pig) exposure (C_{max} and AUC) increases with dose in pigs. Pharmacokinetic parameters [1]:

Dose (mg/kg)	N	C_{max} (g/mL)	T_{max} (h)	T_{last} (h)	$AUC_{0\text{-last}}$ (g.h/mL)	Cl (L/h/kg)	Vss
1	4	2.08 (8)	0.5 [0.5]	[8-48]	11.8 (46)	0.113 (75)	0.5
3	7	8.10 (12)	0.5 [0.5]	[24-72]	42.2 (23)	0.0754 (30)	0.4
10	3	36.7 (5)	0.5 [0.5-0.75]	72	294 (13)	0.0343 (13)	0.3
30	6	112 (27)	0.5 [0.5- 1.0]	[48-72]	908 (16)	0.0338 (18)	0.2

Mean values with (CV%) except T_{max}, which is expressed as median value with [range] and Tlast as [range]. C_{max}, maximum concentration. T_{max}, time at which maximum concentration achieved. T_{last}, last time point sampled. $AUC_{0\text{-last}}$, area under curve from 0 to last time point. Cl, clearance. Vss, volume at steady state or volume of distribution. $T_{1/2z}$, elimination half-life. N, number of animals.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Acute kidney injury rats (12 to 15-week-old Fischer rats)[1]
Dosage:	1 and 3 mg/kg
Administration:	P.o.; administered 1 hour before renal occlusion.
Result:	Inhibited the increase in serum creatinine (89 and 96% at 1 and 3 mg/kg) and urea (61 and 85% at 1 and 3 mg/kg). Protected renal proximal tubules against necrosis and blunted the development of interstitial hemorrhage.

Animal Model:	Acute kidney injury rats (8- to 12-week-old Fischer rats)[1]
Dosage:	3 mg/kg
Administration:	P.o.; twice a day for 7 days and twice a day for 7 day
Result:	Showed a dosedependent trend for reducing macrophage.

REFERENCES

[1]. Bergougnan L, et al. First-in-human study of the safety, tolerability, pharmacokinetics and pharmacodynamics of single and multiple oral doses of SAR247799, a selective G-protein-biased sphingosine-1 phosphate receptor-1 agonist for endothelial protection

[2]. Poirier B, et al. A G protein-biased S1P1 agonist, SAR247799, protects endothelial cells without affecting lymphocyte numbers. Sci Signal. 2020 Jun 2;13(634):eaax8050.

[3]. Evaristi MF, et al. A G-protein-biased S1P1 agonist, SAR247799, improved LVH and diastolic function in a rat model of metabolic syndrome. PLoS One. 2022 Jan 14;17(1):e0257929.

[4]. Bergougnan L, et al. Endothelial-protective effects of a G-protein-biased sphingosine-1 phosphate receptor-1 agonist, SAR247799, in type-2 diabetes rats and a

randomized placebo-controlled patient trial. Br J Clin Pharmacol. 2021 May;87(5):2303-2320.

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