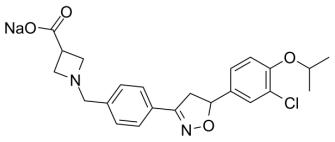
S1P1 agonist 5

Cat. No.:	HY-144126
CAS No.:	2760666-20-2
Molecular Formula:	$C_{23}H_{24}ClN_2NaO_4$
Molecular Weight:	450.89
Target:	LPL Receptor
Pathway:	GPCR/G Protein
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

S1P1 agonist 5 is a selective and orally active S1P1 agonist. S1P1 agonist 5 inhibits the lymphocyte egress from the lymphoid tissue to the peripheral blood. S1P1 agonist 5 has the potential for the research of multiple sclerosis (MS)[1].

In Vitro

S1P1 agonist 5 (compound 21l) shows excellent in vitro efficacies with EC_{50}s of 7.03 nM and 11.8 nM for β-arrestin recruitment and internalization, respectively[1].

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

In Vivo

S1P1 agonist 5 shows good oral bioavaliabily in rats (F=54.2%) and dogs (F=31.8%)[1].

S1P1 agonist 5 (10 mg/kg; p.o.) inhibits the lymphocyte egress from the lymphoid tissue to the peripheral blood and that lymphopenia can be recovered within 24 hours[1].

S1P1 agonist 5 (3, 10 mg/kg, p.o., once daily for 20 days) ameliorates the disease progression and overall severity in EAE mice, showing favorable drug-like properties[1].

Pharmacokinetic Parameters of S1P1 in rats, male beagle dogs[1].

administration	parameters	rat	dog
i.v.	$T_{1/2}$ (h)	1.4±0.3	5.70±1.2
	$AUC_{0-\infty}$ (ng*h/mL)	931.3±95.7	14,830.8±5475.4
	CL (mL/min/kg)	17.6±2.0	149.9±62.5
	V_{ss} (L/kg)	1.7±0.2	828.7±134.2
p.o.	C_{max} (ng/mL)	1661.1±916.6	3979.4±483.5
	T_{max}(h)	0.9±0.8	1.3±0.5
	$T_{1/2}$ (h)	1.4±0.2	4.9±0.6

$AUC_{0-\infty}$ (ng*h/mL)	5044.9±1061	23,109.9±7752.2
F (%)	54.2	31.8

Rats, 1 mg/kg for i.v.; 10 mg/kg for p.o.. dogs, 2 mg/kg i.v.;10 mg/kg for p.o.[1]

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

Animal Model:	rats, male beagle dogs[1]
Dosage:	
Administration:	1 mg/kg for i.v. and 10 mg/kg for p.o (rats); 2 mg/kg for i.v. and 10 mg/kg for p.o.(dogs)
Result:	Showed good oral bioavaliabily in rats (F=54.2%) and dogs (F=31.8%).

Animal Model:	male wistar rats (5 week, 160-180 g)[1]
Dosage:	10 mg/kg
Administration:	p.o.
Result:	Inhibited the lymphocyte egress from the lymphoid tissue to the peripheral blood and that lymphopenia can be recovered within 24 hours.

Animal Model:	female C57BL/6 mice (10 weeks,19−22 g) (experimental autoimmune encephalitis (EAE) mouse model)[1]
Dosage:	3, 10 mg/kg (dissolved in 2.5% DMSO and 5% Kolliphor HS 15 (Sigma-Aldrich) in distilled water)
Administration:	p.o., once daily, 20 days
Result:	Ameliorated the disease progression and overall severity in EAE mice, showing favorable drug-like properties.

REFERENCES

[1]. Park SJ, et al. Discovery of Novel Sphingosine-1-Phosphate-1 Receptor Agonists for the Treatment of Multiple Sclerosis. J Med Chem. 2022; 65(4):3539-3562.

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