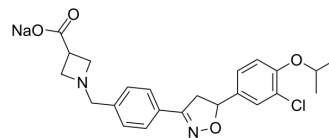


S1P1 agonist 5

Cat. No.:	HY-144126
Molecular Formula:	C ₂₃ H ₂₄ ClN ₂ NaO 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	<p>S1P1 agonist 5 shows good oral bioavailability in rats (F=54.2%) and dogs (F=31.8%)^[1].</p> <p>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].</p> <p>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].</p> <p>Pharmacokinetic Parameters of S1P1 in rats, male beagle dogs^[1].</p> <table border="1"> <thead> <tr> <th>administration</th> <th>parameters</th> <th>rat</th> <th>dog</th> </tr> </thead> <tbody> <tr> <td rowspan="4">i.v.</td> <td>T_{1/2} (h)</td> <td>1.4±0.3</td> <td>5.70±1.2</td> </tr> <tr> <td>AUC_{0-∞} (ng*h/mL)</td> <td>931.3±95.7</td> <td>14,830.8±5475.4</td> </tr> <tr> <td>CL (mL/min/kg)</td> <td>17.6±2.0</td> <td>149.9±62.5</td> </tr> <tr> <td>V_{SS} (L/kg)</td> <td>1.7±0.2</td> <td>828.7±134.2</td> </tr> <tr> <td rowspan="3">p.o.</td> <td>C_{max} (ng/mL)</td> <td>1661.1±916.6</td> <td>3979.4±483.5</td> </tr> <tr> <td>T_{max}(h)</td> <td>0.9±0.8</td> <td>1.3±0.5</td> </tr> <tr> <td>T_{1/2} (h)</td> <td>1.4±0.2</td> <td>4.9±0.6</td> </tr> </tbody> </table>			administration	parameters	rat	dog	i.v.	T _{1/2} (h)	1.4±0.3	5.70±1.2	AUC _{0-∞} (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
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AUC_{0-∞} (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 bioavailability 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.

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

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