CXCR7 modulator 2

Cat. No.: HY-112154

CAS No.: 2227426-37-9

Molecular Formula: $C_{29}H_{42}N_6O_3$

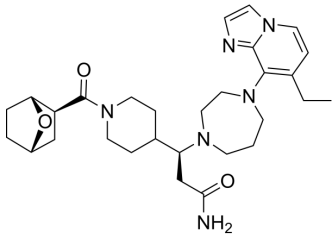
Molecular Weight: 522.68

Target: CXCR

Pathway: GPCR/G Protein; Immunology/Inflammation

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 250 mg/mL (478.30 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.9132 mL	9.5661 mL	19.1322 mL
	5 mM	0.3826 mL	1.9132 mL	3.8264 mL
	10 mM	0.1913 mL	0.9566 mL	1.9132 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: ≥ 2.08 mg/mL (3.98 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (3.98 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (3.98 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

CXCR7 modulator 2 is a modulator of C-X-C Chemokine Receptor Type 7 (CXCR7), with a K_i of 13 nM.

IC_{50} & Target

CXCR7
13 nM (Ki)

In Vitro

CXCR7 modulator 2 (compound 18) demonstrates potent CXCR7-binding affinity (K_i=13 nM) and β-arrestin activity (EC_{50}=11 nM). CXCR7 modulator 2 also exhibits improved selectivity in the GPCR panel and an improved therapeutic index in the hERG

	patch-clamp assay in comparison with 11c. CXCR7 modulator 2 exhibits moderate to high in vitro turn over in both NADPH-supplemented mouse-liver microsomes (MLM, 93 μL/min/mg) and hepatocytes (28 μL/min per million cells), shows poor passive absorptive permeability in the MDCK II-permeability assay, and has good aqueous solubility. CXCR7 modulator 2 is rapidly absorbed with a mean maximal plasma concentration (C_{max}) of 682 ng/mL, which occurrs at 0.25 h (T_{max}). The corresponding mean area under the plasma-concentration-versus-time profile (AUC) is 740 ng/mL/h[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	The administration of isoproterenol for 9 days leads to the development of cardiac fibrosis, as attested by the approximately 4-fold increase in collagen deposition relative to that in the control, which is detected by picrosirius-red staining. Treatment with CXCR7 modulator 2 results in a statistically significant reduction in cardiac fibrosis, thereby demonstrating the protective role of CXCR7 modulation with CXCR7 modulator 2 in an isoproterenol-induced cardiac injury[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	Measurements of potassium currents in HEK293 cells are stably transfected with the hERG channel[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice[1] A total of 60 male BALB/c mice (8 weeks of age) are randomized into four study groups. In two groups, isoproterenol (5 mg/kg) is administered subcutaneously once daily for 9 days to induce cardiac fibrosis. In addition, the mice in these two groups are further treated twice daily throughout the 9 day study duration with either CXCR7 modulator 2 at 30 mg/kg (n=20) or the vehicle (n=20). The mice in the third group receives PBS and the vehicle and thus serves as controls (n=15). The fourth group (n=5), which receives both isoproterenol and CXCR7 modulator 2, are used for blood sampling at 1 and 9 h postdose on days 1, 3, 6, and 9 (1 h only) to provide an overall estimate of CXCR7 coverage relative to mouse K_i. The exposures to CXCR7 modulator 2 achieved in the BALB/c mice at the 30 mg/kg dose are approximately as expected, with the unbound Cave>95% target coverage[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Menhaji-Klotz E, et al. Discovery of a Novel Small-Molecule Modulator of C-X-C Chemokine Receptor Type 7 as a Treatment for Cardiac Fibrosis. J Med Chem. 2018 Apr 26;61(8):3685-3696.

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